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VISUALIZATION OF THE AORTA AND ITS BRANCHES BY RETROARTERIAL DIODRAST INJECTION

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RADIOGRAPHIC visualization of the heart and great vessels following intravenous injection of Diodrast is an established procedure.[1-15] In order to obtain diagnostic radiograms, the Diodrast must be injected very rapidly, so that it is present in the heart and great vessels in sufficient concentration to produce a sharply outlined shadow. This technique has been described previously[16] and excellent visualization of the entire right side of the heart and pulmonary arteries has been thus obtained. With dispersion of the Diodrast throughout the pulmonary circulation and its subsequent return to the left auricle, good visualization of the left auricle, left ventricle, and aorta is usually obtained. However, the radiograms are frequently not as good as those of the right side of the heart, and the aorta in particular is often indistinctly outlined.

For these reasons it has been felt that injection of Diodrast directly into the aorta would result in more clearly defined radiograms of the aorta and large arteries. Direct puncture of the abdominal aorta through the paravertebral region has been advocated by dos Santos[17] and later by Wagner.[18] Fariñas[19] developed a technique of catheterizing the femoral artery in the region of Scarpa's triangle and, by manipulation, passing the catheter tip upward to any desired level in the aorta before injecting the opaque material. In an effort to improve these techinques, it was felt that retroarterial injection of opaque material through an artery which originates from the aortic arch would more completely outline the whole length of the aorta. Castellanos[20] has used the brachial artery for retrograde injections in diagnosing both coaretation of the aorta and patent ductus arteriosus. Clarence Crafoord[21] uses essentially the same technique. Instead of making the injection along the whole length of the artery, he prefers to insert a catheter up the artery until the catheter tip reaches the aorta. The injection of opaque material is then made

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through the catheter. Use of the left common carotid artery has been considered because a larger amount of Diodrast can be more rapidly injected into the aorta. Norman Freeman[22] has used it successfully in the diagnosis of both coarctation of the aorta and patent ductus arteriosus. In children we consider the left common carotid artery best suited for this procedure, and this vessel has been used in all of our studies.

TECHNIQUE

All patients are given a general ether anesthesia. Preoperative care is the same as that given to any patient who is to receive a general anesthetic. Using sterile surgical precautions, an incision is made in the left supraclavicular area directly over the left common carotid artery. Dissection is carried down to the carotid sheath, which is opened, and the internal jugular vein and vagus nerve are identified. The carotid artery is exposed, and three heavy, braided, silk ligatures are passed around the artery but not tied.

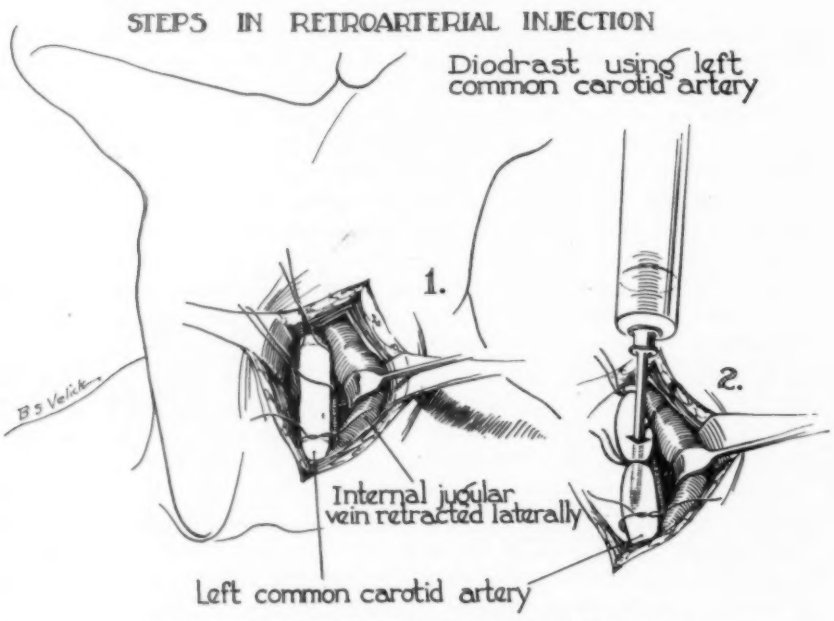

Fig. 1.—Drawing showing steps in retroarterial injection.

The patient is then placed on the tautograph[23] in the right posterior oblique position, In very rapid sequence the upper ligature is tied to prevent cephalad reflux of the dye. The lowermost of the three ligatures is tied loosely at a point approximately one inch below the uppermost ligature. A small incision is made transversely in the vessel wall, and a No. 10 cannula introduced

with the tip extending toward the heart. The third ligature is tied around the vessel just below the opening in the vessel wall and over the shaft of the cannula. This ligature prevents blood leakage. The lowermost tie is loosened, and 30 c.c. to 50 c.c. of 70 per cent Diodrast are injected very rapidly after the tautograph has been started. The lowermost ligature is again tightened and the middle ligature loosened. The cannula is withdrawn and the small opening in the vessel wall sutured with 00000 silk on a nontraumatic needle. The short incision in the neck is repaired in the usual manner. The technical steps are illustrated in Fig. 1.

With this type of injection we have seen much less change in respiration than is seen following intravenous injection of Diodrast. Attempts to utilize the brachial artery have given disappointing results. It is extremely difficult to inject retroarterially over such a long column a sufficient quantity of dye with the rapidity necessary to give sharp delineation of the aorta and its branches.

RESULTS

To date we have studied two types of lesions by this method: patent ductus arteriosus and coarctation of the aorta.

CASE 1.—W. J. F., a 7-year-old girl, was admitted because of a suspected patent ductus arteriosus. On examination a rough "machinery murmur" was audible in the second left interspace, accompanied by a palpable thrill. The blood pressure was 135/72. Fluoroscopy revealed increased pulmonary vascular markings with a heart of normal size. The pulmonary conus was quite prominent.

Retrograde arterial Diodrast studies were performed through the left common carotid artery with radiograms as illustrated in Figs. 2 and 3. Fig. 2 shows Diodrast filling the ascending aorta and aortic arch. In Fig. 3 the whole aorta is well outlined. The pulmonary artery can be seen just anterior to the first part of the descending aorta. The patent ductus can be seen connecting these two structures.

CASE 2.—H. M., a 4-year-old boy, was admitted with a diagnosis of patent ductus arteriosus. On examination all of the classical findings of this condition were present. Retrograde arterial Diodrast studies were performed. In Fig. 4 the descending aorta and a portion of the aortic arch are clearly visualized. Both left and right pulmonary arteries are well filled with opaque material. The patent ductus was subsequently obliterated by operation.

CASE 3.—R. P., a 21-year-old woman, was admitted for study because of a suspected coarctation of the aorta. Preceding studies had revealed slight lowering of systolic blood pressure and a slight decrease in capillary arterial pulsations in the lower extremities. No hypertension was present in the upper extremities.

Retrograde arterial studies were performed. In Fig. 5 the whole aorta is well visualized. A slight constriction of the aorta is seen just distal to the origin of the left subclavian artery.

CASE 4.—G. B., a 14-year-old boy, was admitted because of increasing dyspnea on exertion and easy fatigability during the past year. The important features noted on examination were as follows: A loud systolic murmur accompanied by a systolic thrill was present over the base of the heart with maximum intensity over the aortic area; pulsations of the femoral and dorsalis pedis arteries were weak. Blood pressure studies were: Right arm 127/96, left arm 130/94, right leg 120/84, left leg 124/80. Special studies revealed a decreased blood flow and a decrease in arterial pulsation in the lower extremities as compared to the upper extremities.

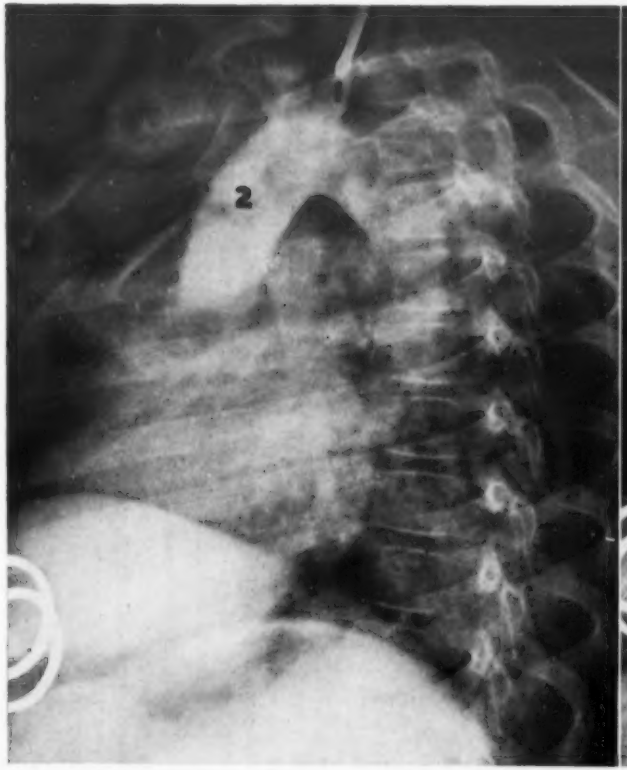

Fig. 2.

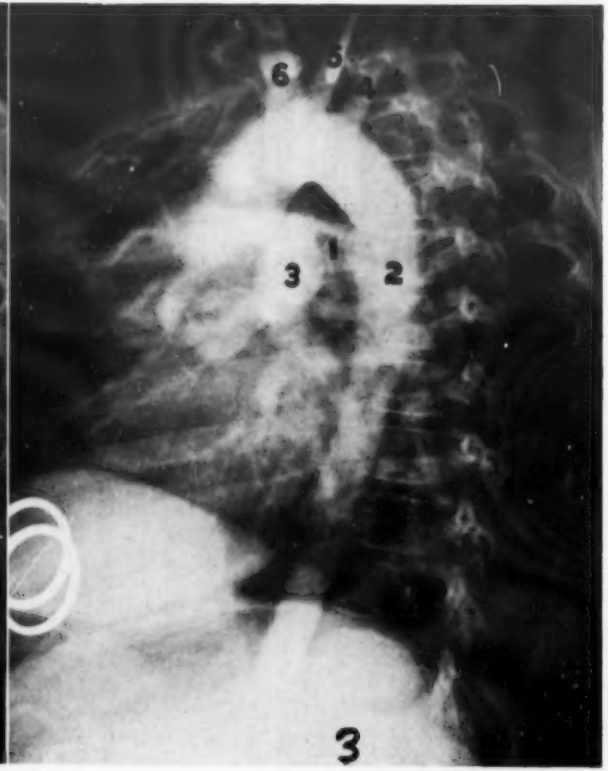

Fig. 3.

Fig. 2.—Left anterior oblique radiogram. *1*, Left common carotid artery. *2*, Ascending aorta.

Fig. 3.—Left anterior oblique radiogram. *1*, Patent ductus arteriosus. *2*, Descending aorta. *3*, Pulmonary artery. *4*, Left subclavian artery. *5*, Left common carotid artery. *6*, Innominate artery.

clavian artery. 5, Left common carotid artery. 6, Innominate artery.

Fig. 4. Fig. 5.

Fig. 4.—Left anterior oblique radiogram. *1*, Left common carotid artery. *2*, Descending aorta. *3*, Left pulmonary artery. *4*, Right pulmonary artery.

Fig. 5.—Left anterior oblique radiogram. *1*, Very slight indentation in anterior wall of descending aorta.

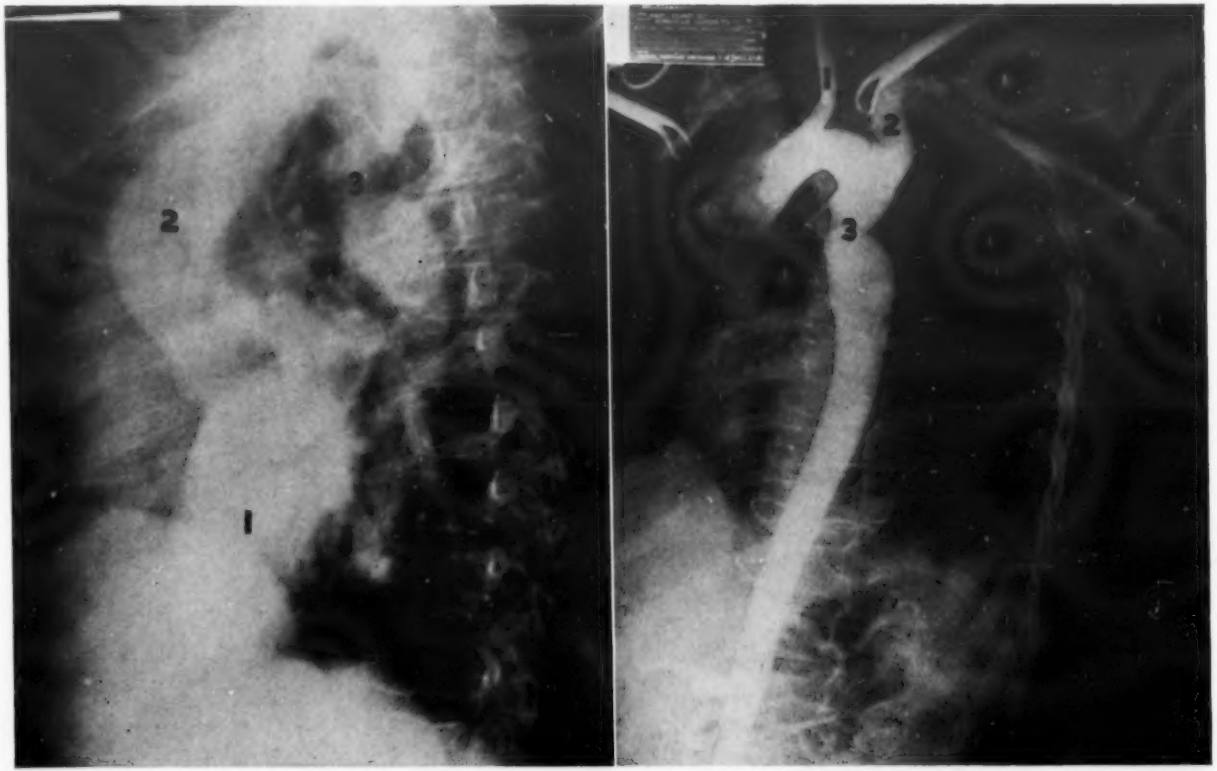

Fig. 6. Fig. 7.

Fig. 6.—Left anterior oblique radiogram. *1*, Left ventricle. *2*, Ascending aorta. *3*, Point of constriction of descending aorta.
Fig. 7.—Left anterior oblique radiogram. *1*, Left common carotid artery. *2*, Left subclavian artery. *3*, Point of constriction of descending aorta.

An angiocardiogram was done with 70 per cent Diodrast injected intravenously. Fig. 6 shows one of the last of ten radiograms taken at one-second intervals following the injection. The left auricle, left ventricle, and ascending aorta are well visualized. There appears to be a constriction of the aorta in the midportion of the aortic arch. Just distal to this is a second point of constriction and angulation.

A retrograde arterial study was performed two days later. In Fig. 7 the aortic arch appears well filled with Diodrast. There is slight narrowing of the aorta between the left common carotid artery and the left subclavian artery. Just distal to the left subclavian artery is a sharp constriction. Comparison of Figs. 6 and 7 demonstrates the superiority of the radiograms made with the retroarterial procedure.

Although the constricted area is very narrow in length, it was felt this patient should not have a corrective operation because of the absence of hypertension and because the coarctation was not of sufficient severity to interfere seriously with the flow of blood through the aorta.

CASE 5.—N. P., an 8½-year-old white girl, was admitted with an acute recurrence of rheumatic fever. The most important physical findings were as follows: There were marked suprasternal and carotid pulsations; the heart was enlarged to the left with a systolic and diastolic murmur present over the apical region and also over the second and third right and left interspaces. Capillary pulsations and a Corrigan pulse were noted. A loud, systolic murmur was present over the scapular region. Blood pressure readings were as follows: right arm 180/110, left arm 110/70, right leg and left leg not obtainable. Special studies revealed a decreasd blood flow and decreased arterial pulsations in both lower extremities.

An intravenous angiocardiogram was done. Only fair visualization of the ascending aorta was obtained with no clear definition of the coarcted segment. A retrograde arterial study was performed as illustrated in Figs. 8 to 11. In Fig. 8 the ascending aorta and left common artery are seen. In Fig. 9 a sharp constriction is seen at the beginning of the descending aorta. The innominate, right subclavian, and internal mammary arteries are well visualized. The coronary artery may be seen just posterior to the first part of the ascending aorta. Fig. 10 reveals the same structures as were just described and in addition shows some of the extensive collateral circulation. The left subclavian artery arises from the distal part of the constricted segment opposite. In Fig. 11 the aortic arch is seen empty of opaque material, although the descending aorta is still filled.

The clinical diagnoses in this patient were: (1) coaretation of the aorta, (2) mitral stenosis and insufficiency, (3) aortic insufficiency.

CASE 6.—W. W., a 15-year-old boy, was hospitalized for investigation of hypertension. His subjective complaints were severe headaches and blurring of vision following exercise. Physical examination revealed a systolic and diastolic murmur over the base of the heart. The blood pressure was: right arm 165/105, left arm 160/100, right leg 100/90, left leg 95/90. Pulsations of the abdominal aorta and femoral arteries were very feeble. Notching of the ribs was demonstrated by roentgenography.

Retroarterial injection of Diodrast was carried out, using the left common carotid artery. Serial roentgenograms taken following the injection are seen in Figs. 12 to 15. Fig. 12 reveals early visualization of the aortic arch, innominate artery, and left subclavian artery. In Fig. 13 the coarcted segment of aorta can be seen just distal to the origin of the left subclavian artery. A network of dilated deep arteries of the neck can be seen arising from the left subclavian artery and anastomosing with a dilated intercostal artery arising from the aorta distal to the coarctation. Dilated internal mammary arteries and the left subscapular artery are clearly seen. In Fig. 14 the aortic arch is no longer seen. The site of coarctation and the descending aorta are still visualized. Note the extensive collateral circulation. Fig. 15 demonstrates the dilated intercostal arteries.

Fig. 8.

Fig. 9.

Fig. 8.—Left anterior oblique radiogram. *1*, Ascending aorta. *2*, Left common carotid artery.
Fig. 9.—Left anterior oblique radiogram. *1*, Innominate artery. *2*, Constricted segment of aorta. *3*, Coronary artery.

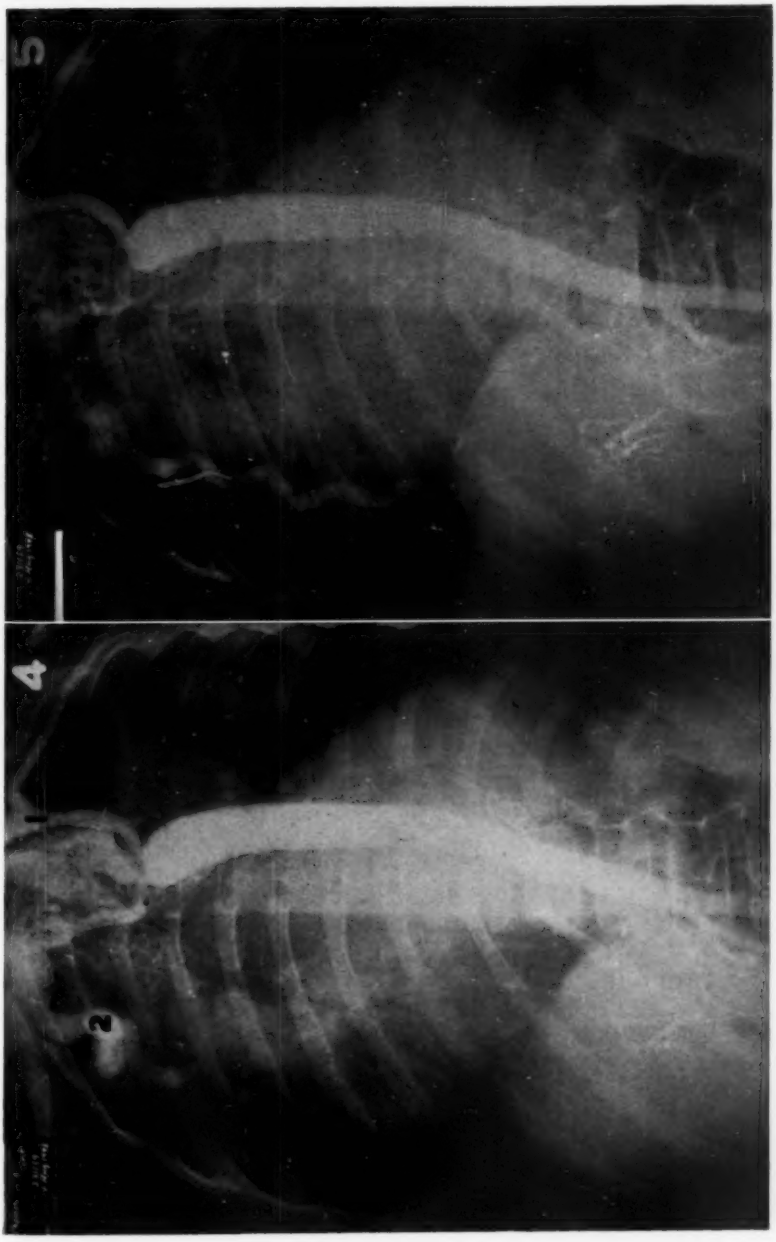

Fig. 10. Fig. 11.

Fig. 10.—Left anterior oblique radiogram. *1*, Left subclavian artery. *2*, Internal mammary artery.
Fig. 11.—Left anterior oblique radiogram.

Fig. 12.

Fig. 13.

Fig. 12.—Left anterior oblique radiogram. *1*, Ascending aorta. *2*, Innominate artery. *3*, Left common carotid. *4*, Left subclavian artery.

Fig. 13.—Left anterior oblique radiogram. *1*, Right subclavian artery. *2*, Right internal mammary artery. *3*, Right innominate artery. *4*, Left common carotid. *5*, Left subclavian artery. *6*, Point of coarctation of the aorta. *7*, Left subscapular artery. *8*, Left internal mammary artery. *9*, Epigastric artery.

ternal mammary artery. 9, Epigastric artery.

Fig. 14.—Left anterior oblique radiogram.

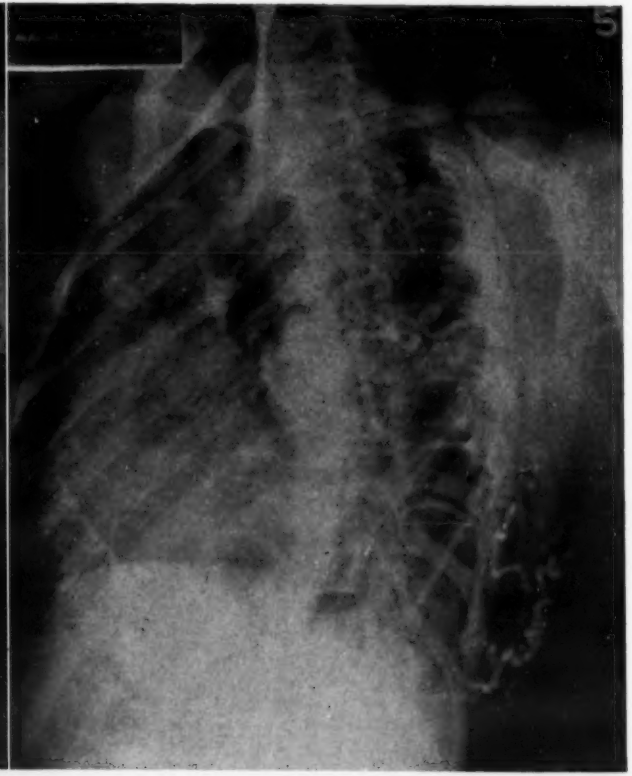

Fig. 15.—Left anterior oblique radiogram.

DISCUSSION

The technique of retroarterial injection of radiopaque material for visualization of the aorta and its branches is a safe and valuable complement to intravenous injection for visualization of the heart and pulmonary circulation. This procedure may be employed to establish the diagnosis of an arteriovenous shunt between the aorta and pulmonary circulation. In some cases a patent ductus arteriosus may actually be visualized. When the ductus is not seen, filling of the pulmonary arteries simultaneously with filling of the aorta is proof that a direct shunt exists.

When surgery is contemplated in patients with coaretation of the aorta, the point of constriction may be definitely localized in this manner. Unless a complete aortic atresia is present, it is also possible to determine preoperatively whether or not the constricted segment is sufficiently localized to allow surgical resection and anastomosis.

Other congenital anomalies of the aorta such as aortic "ring," or aberrant vessels with tracheal or esophageal compression can, we are certain, be clearly demonstrated by this method. So far we have not had an opportunity to visualize a case of this type. We have definitely been able to rule out aneurysms of the aorta in this way.

It is fortunate that the large field of applicability of this procedure is in the younger age group. It should be pointed out that utilization of the carotid, even though the procedure is a temporary one, is fraught with some hazard in adults. One can, we believe, use the carotid artery very safely in children. In the group of eight patients which have been studied, we have had no complications and no manifestations to suggest that there had been interference, even temporarily, with adequate blood supply to the brain.

CONCLUSIONS

A method of retroarterial Diodrast injection for the visualization of anomalies or disease of the aorta and its immediate branches is presented. Utilization of the left common carotid artery has proved satisfactory. This method provides a safe, dependable, and effective means of diagnosing questionable cases of patent ductus arteriosus, coaretation of the aorta, and aortic arch anomalies, and is useful in proving or disproving selected cases of aneurysms.

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ELECTROPHORETIC STUDIES OF PLASMA AND URINARY PROTEINS IN CHILDREN WITH LIPOID NEPHROSIS

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INTRODUCTION

As a part of an extensive series of clinical and chemical studies of lipoid nephrosis in children, electrophoretic analysis of the plasma and urine appeared to offer a source of valuable data concerning the distribution of the protein fractions in this disease. In recent years, electrophoresis has been applied to a study of the plasma proteins in various diseases.[1] Several cases of nephrosis have been discussed in these studies, but none of the investigators has been primarily concerned with nephrosis in children. In 1939, Longsworth and MacInnes[2] observed abnormal electrophoretic patterns of the plasma and urine of two nephrotic patients, whose ages were not given. The plasma and urinary proteins of several patients with nephrosis, three of whom were children, have been studied electrophoretically by Luetscher.[3, 4, 5] Also Thorn and associates[6] have made similar studies of seven adults in the nephrotic stage of chronic nephritis during treatment with concentrated serum albumin. Studies of two children with lipoid nephrosis were included in a series of investigations by Janeway and his co-workers.

The present study concerns an electrophoretic analysis of the plasma and urine of children with lipoid nephrosis. For five children the studies were made before, during and after treament with concentrated, salt-poor human serum albumin.*

PROCEDURE

Plasma or urine samples were diluted with buffer to a protein concentration of 1.5 to 2.0 per cent and dialyzed at 2 to 6° C. for three days with daily change of buffer.

The buffer solution was 0.1 normal sodium diethyl barbiturate with a pH of 8.6 and an ionic strength of 0.1. Electrophoresis of the dialyzed plasma was performed at 0.8° C. in the apparatus described by Tiselius[8] using the long center section cell. The Schlieren scanning device of Longsworth[9] was used to obtain Schlieren diagrams of the plasma proteins. Tracings of the diagrams were prepared by projecting the photographic negatives magnified two and one-half times on a glass screen. Patterns from the descending boundaries were then analyzed according to the following methods. The components were

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*The serum albumin used in this study was processed by the American National Red Cross from blood which it collected from voluntary donors.

This is one of a series of investigations on serum albumin being carried out with material supplied by the American National Red Cross. As soon as sufficient data become available to justify final conclusions concerning its therapeutic value, a full report to the medical profession on the use of serum albumin in medical practice will be published by the Committee on Blood and Blood Derivatives of the Advisory Board on Health Services of the American National Red Cross.

resolved by the method of Pedersen[10] and the area of each component determined by planimetric measurement. The percentage composition of the plasma proteins was calculated by comparing the area of each component with the total area of the tracing. Electrophoretic mobilities of the various components were calculated from the distance the component moved during electrophoresis, the current, time, the cross-section area of the cell, and the conductivity of the protein solution.

Some of the plasma samples contained suspended fat globules which scattered the light and interfered with photography of the Schlieren diagrams. Centrifugation in the cold at 5,500 r.p.m. was used in an attempt to clarify several of these samples. Photographic compensation involving the use of light filters and increased illumination was also employed to overcome this interference. If these methods were unsuccessful, the data from these samples were discarded.

It was realized that the so-called β-globulin disturbance present in the majority of the plasma patterns was caused by lipoproteins in clear solution in the plasma which migrate at approximately the same rate as the α_2- and β-globulins. Since extraction of the plasma with fat solvents removed an unknown quantity of this characteristic lipoid material as well as the suspended fat,[2] this method was not employed to clarify the plasma samples containing fat.

DISTRIBUTION OF PROTEINS IN NEPHROTIC SERA

The data for the percentage composition of the plasma proteins and the total protein concentration in grams per 100 ml. plasma are shown in Table I. For purposes of comparison, we have included average values for percentage composition of the plasma of thirteen normal children.[11] Total protein concentration was determined by a colorimetric micro-Kjeldahl method.

The changes in the percentage composition of the plasma proteins in nephrosis were very striking. Abnormal variations in albumin, α_1-, α_2-, and β-globulins occurred in all stages of the disease. As noted by others previously[1, 2, 3, 6] the albumin concentration was markedly reduced, while the α- and β-globulins were increased. With prolongation of the disease, variations from the normal pattern became more marked. The concentration of albumin was further reduced and in most instances the α_2- and β-globulin content increased as the albumin decreased. See, for example, in Table I the figures for G. S., compared with those for S. S., before and after recovery from nephrosis. Patient S. S. was ill only a short time, developed measles, had only moderate edema, and recovered promptly. The electrophoretic pattern of her plasma proteins showed a decrease in albumin, an increase in β-globulin, only a slight elevation in α_2-globulin, and normal α_1-globulin concentrations. Patient G. S. had been chronically ill for eleven months with marked ascites requiring repeated paracenteses. The albumin concentration in his plasma was greatly reduced, the β- and α_2-globulin concentrations greatly elevated, and α_1-globulin concentration normal or increased.

In some cases, the α_1-globulin concentration also increased concomitantly with the α_2- and β-globulins, e.g., H. A., on March 3, 1947. In others, e.g., H. A.,

TABLE I. ELECTROPHORETIC ANALYSES OF PLASMA PROTEINS OF CHILDREN WITH NEPHORSIS

SUBJECT	SEX AND AGE	DATE	ALBUMIN THERAPY	TOTAL PROTEIN (GM./100 ML.)	PERCENTAGE COMPOSITION					
					ALB.	GLOBULINS				
					A	α_1	α_2	β	ϕ	γ
I. Severe Edema and Ascites Requiring Frequent Paracenteses for Several Months										
G. S.	M 3	7/19/46	None	3.6	2.5	3.5	45.0	33.8	12.5	2.7
		7/27/47	5 c.c. γ-globulin i.m. 7/19 to 7/26	4.4	6.2	3.1	26.7	44.2	15.6	4.2
		10/29/46	None	3.8	7.8	6.5	30.4	32.6	7.4	15.2
		11/19/46	None	6.0	1.4	21.8	25.8	28.0	9.6	13.4
D. M.	M 3	6/21/46	None	4.5	5.3	3.2	47.9	20.7	19.7	3.2
		6/22/46	25 Gm.	4.9	4.7	9.9	56.7	16.4	11.7	0.6
		6/23/46	25 Gm.	4.5	9.8	13.6	48.8	17.5	9.8	0.5
		6/24/46	25 Gm.	4.5	9.9	9.9	53.2	17.6	6.4	3.0
		6/25/46	None	4.4	12.1	19.1	35.0	16.1	13.4	4.3
		11/19/46	None	4.6	13.3	27.5	34.4	7.1	14.4	3.3
J. W.	F 3	6/17/46	None	5.5	6.8	6.1	28.0	39.4	17.4	2.3
		6/18/46	After 20 Gm.	5.2	8.1	11.0	46.2	17.6	13.8	3.3
		11/19/46	None	5.0	12.2	29.4	31.0	10.0	15.0	2.4
		4/24/47	25 Gm. daily	4.8	13.2	13.2	35.1	21.5	13.2	3.7
		5/15/47	4/24 to 6/1	5.9	47.3	3.3	25.9	14.9	6.4	2.2
J. O.	F 3	7/24/47	25 Gm. daily	4.5	9.3	20.4	38.7	13.7	14.7	3.2
		9/3/47	7/25 to 9/15	6.3	30.1	18.5	26.8	6.5	15.3	2.8
		10/1/47	None	4.3	4.4	28.1	34.0	10.7	15.9	6.9
		10/22/47	None	5.1	9.3	5.0	61.6	10.6	11.1	2.4
T. V.	M 2	10/27/47	None	4.5	12.2	26.0	41.1	10.2	9.8	0.7
H. A.	M 7	10/28/46	None	4.2	16.7	3.6	28.2	30.7	7.9	12.9
		3/3/47	None	4.9	5.8	15.1	35.0	30.2	9.8	4.1
		3/13/47	25 Gm. daily	4.4	17.4	4.6	38.9	22.2	10.5	6.4
		4/15/47	3/3 to 5/1	5.1	16.2	5.8	49.2	12.1	11.6	5.1
		5/2/47		4.9	21.7	4.1	38.2	21.6	10.6	3.9
		5/15/47	25 Gm. daily	4.0	20.5	26.0	33.8	7.2	9.8	2.7
		6/19/47	5/19 to 6/17	4.5	18.3	3.8	38.0	22.7	11.2	6.0
		7/29/47	None	5.1	16.8	31.5	31.1	7.2	8.7	4.7
II. Moderate Edema, Ascites not Severe										
R. H.	M 4	11/19/46	None	4.8	22.3	26.4	32.2	6.2	6.1	6.8
C. T.	F 8	5/9/47	25 Gm. daily	5.4	19.8	23.3	30.0	8.5	15.8	2.6
		5/27/47	5/19 to 6/3	5.2	38.5	4.6	21.6	22.7	8.0	4.6
		6/19/47	None	4.3	16.4	9.2	34.8	20.8	14.5	4.3
III. Early Stage of Disease with Minimum Edema										
R. D.	M 3	11/19/46	None	5.6	21.7	2.4	18.3	28.2	9.0	10.4
S. S.	F 4	7/10/46	None	8.2	32.9	4.3	13.8	29.8	10.8	8.4
		7/13/46	After 25 Gm.	6.9	39.1	2.6	13.3	31.1	7.1	6.8
IV. Completely Recovered										
S. S.	F 4	6/24/47	None (recovered)	7.9	60.6	6.5	8.9	12.6	4.1	7.3
J. K.	M 3	4/29/47	None (recovered)	8.0	57.3	8.0	11.3	11.3	5.0	7.1
Average values for thirteen normal children (3-8 years)				7.5	57.7	6.3	10.6	10.3	5.2	9.7

on May 15, 1947, and D. M., on Nov. 19, 1946, α_1-globulin appeared to be increased at the expense of β-globulin.

The fibrinogen fraction also exhibited a fairly regular increase as the albumin decreased. The γ-globulin content of the plasma of the majority of the nephrotic children was definitely lower than that of the plasma of normal children of the same age.

Schlieren diagrams of representative plasma samples are illustrated in Figs. 1 to 4. Fig. 1 shows the electrophoretic pattern from the plasma of a normal child. Fig. 2 shows the pattern obtained by electrophoresis of the

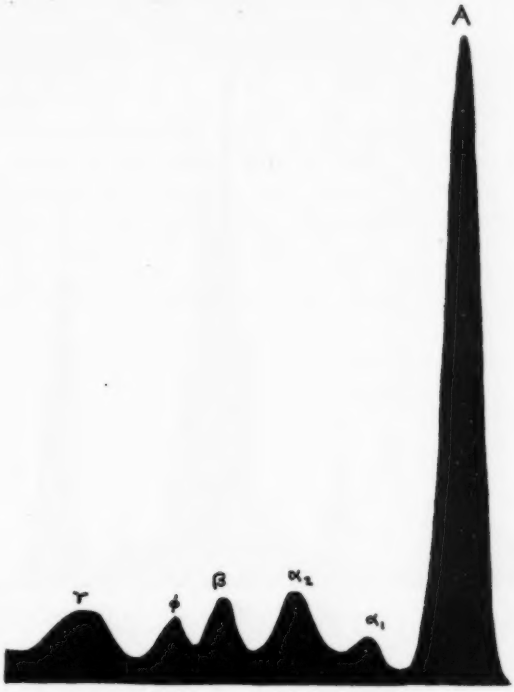

Fig. 1.—Plasma from a normal 4-year-old boy.

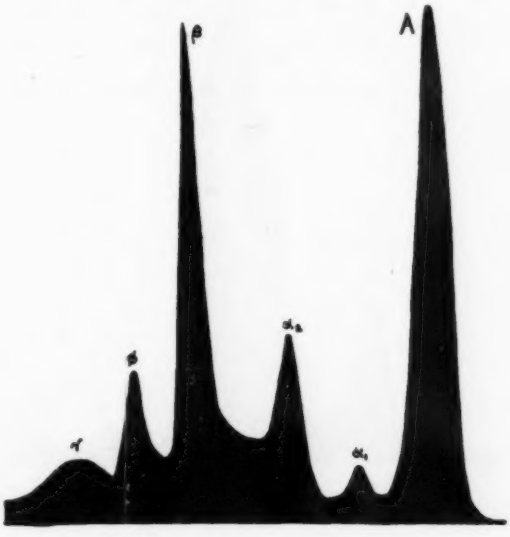

Fig. 2.—Plasma from a 4-year-old girl, S. S., with nephrosis of two months' duration. Edema had been minimal for the previous month.

Fig. 3.—Plasma from R. D., a 3-year-old boy with nephrosis for the previous nine months. Edema was not marked at the time the blood sample was analyzed.

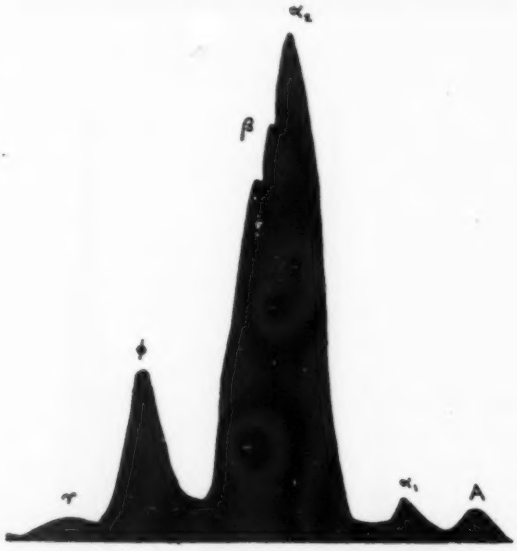

Fig. 4.—Plasma from G. S., a 2-year-old boy with nephrosis for eleven months. The child had severe edema and ascites requiring frequent paracenteses and was very ill at the time of the plasma analysis.

plasma of a nephrotic child early in the course of the disease (S. S., July 26, 1946). The albumin content has decreased to 39 per cent and the β-globulin content is abnormally high. A further decrease in the albumin and an increase in the β-globulin disturbance may occur in later stages of this chronic disease. For example, the pattern for R. D., Nov. 25, 1946 (Fig. 3), who had been ill for nine months, shows a decrease in albumin to 22 per cent and a very pronounced α_2- and β-globulin disturbance. Even greater decreases in albumin, to as little as 2.5 per cent of the total proteins with corresponding increases in globulin, have been noted when the child has been seriously ill for many months with pronounced edema and marked undernutrition. (See Fig. 4, G. S., July 29, 1946.)

In analyzing the tracings from Schlieren diagrams which are as abnormal as those obtained from plasma of nephrotic children, the mobility measurements are very important. These measurements were made for every pattern that was analyzed but the data are not included in the tables reported here. The distance a component has moved during electrophoresis is an essential value in establishing the location of the area on the pattern caused by a specific protein component. The mobility measurements of the plasma proteins for any one patient show normal variation from one determination to the next. When the values for the plasma proteins in nephrosis are compared with those from normal children of the same age, there appears to be a slight decrease in mobility of each protein component, but this decrease is of questionable significance.

Data from the electrophoretic analyses of urinary and body fluid proteins from nephrotic children are shown in Table II. The electrophoretic patterns of most of the urine samples were similar to that shown in Fig. 5. The protein

TABLE II. ELECTROPHORETIC ANALYSES OF URINE AND BODY FLUIDS OF CHILDREN WITH NEPHROSIS

SUBJECT	SEX AND AGE	DATE	ALBUMIN THERAPY	TOTAL PROTEIN	PERCENTAGE COMPOSITION					
					ALB.	GLOBULINS				
					A	α_1	α_2	β	ϕ	γ
Urine (Gm./day)										
H. A.	M 7	3/1/47	None	12.8	43.9	19.5	10.2	9.3		17.1
		4/5/47	25 Gm. daily	29.0	79.9	11.8		4.5		3.8
		4/30/47	3/3 to 5/1	34.8	87.0	9.2		3.8		
D. M.	M 3	6/21/46	None	8.4	72.1	21.0		6.9		
		6/22/46	25 Gm.	17.9	88.2	9.1		2.8		
		6/23/46	25 Gm.	18.5	89.0	7.6		3.4		
		6/24/46	25 Gm.	11.3	92.3	5.2		2.6		
		6/25/46	None	4.1	88.9	8.5		2.7		
S. S.	F 4	7/10/46	None	1.1	89.9	6.9		3.3		
		7/11/46	After 25 Gm.	3.9	69.7	7.1	8.9	14.3		
		7/13/46	None	1.3	84.6	3.8				11.5
J. W.	F 3	6/18/46	After 20 Gm.	11.7	71.0	17.2		8.6		3.2
Body Fluids (Gm./100 ml.)										
H. A.	M 7	3/2/47	None	0.10	24.3	14.2	27.0	8.9	14.2	11.3
(ascitic fluid)		10/28/47	None	0.59	16.2	11.9	34.3	8.7	11.4	17.6
(pleural fluid)		3/2/47	None	0.19	15.7	7.3	42.6	6.3	15.3	12.8
T. V.	M 2	8/14/47	25 Gm. daily for 21 days	0.26	54.1	7.6	27.5	5.4	3.0	2.4
(ascitic fluid)										

components present in these samples were identified by calculation of their mobilities. The two globulin components common to every sample were α_1- and β-globulin. In a few samples α_2- or γ-globulins were present, and in one case (H. A., March 4, 1947) all of the components of plasma, except fibrinogen, were present.

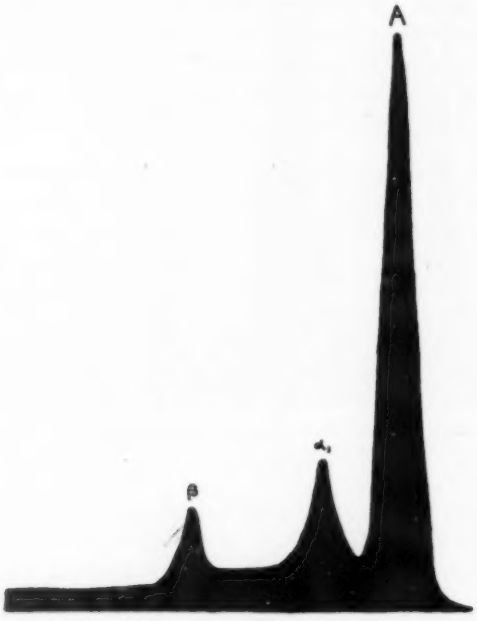

Fig. 5.—Urine from D. M., a 3-year-old boy, severely ill with nephrosis for eleven months. The child had marked edema and ascites requiring frequent paracenteses at the time of the study.

The ascitic and pleural fluids from H. A. and T. V. were very low in protein content. Before analysis they were concentrated by fanning them in Visking casings. Electrophoretic analysis of the fluids from H. A. gave values for protein fractions that were similar to those obtained from his plasma, although in every case the fluid contained a lower percentage of β-globulin and a somewhat higher percentage of albumin than the plasma. The ascitic fluid from T. V. contained a much higher percentage of albumin than the plasma, although these samples were drawn at such different dates that they are not strictly comparable. The plasma sample that was collected the same day the fluid was drawn was so lipemic that the pattern could not be analyzed.

EFFECTS OF ADMINISTRATION OF CONCENTRATED HUMAN SERUM ALBUMIN

Early in this study it was believed that the more accurate definition of the plasma proteins by electrophoretic analysis might be useful in following the effects of therapy. Concentrated human serum albumin was injected intravenously in several children in an attempt to increase the albumin content of

their plasma to a sufficiently high level to overcome the edema and improve their clinical condition. Usually 25 Gm. of albumin were injected daily. At first the effects of one day's administration (See Table I, J. W., June 18, 1946, and S. S.) and three consecutive daily injections (D. M.) were studied. Even though the percentage of albumin in D. M.'s plasma more than doubled during the treatment (5.3 to 12.1 per cent) no clinical improvement was observed. These results are similar to those observed by Luetscher,[5] who studied the effects of a single dose of albumin in nephrotic patients. Other children were then given daily injections for as many as sixty days or a total of 1,500 Gm. albumin. The response to these larger doses varied with the child. No striking changes in plasma albumin were noted in H. A., although he received a total of 2,250 Gm. of albumin in two periods of treatment. After an initial increase from 5.8 to 17.4 per cent, the albumin content did not rise above 22 per cent. Three other children (J. W., J. O., and C. T.) showed a better response and marked increase in plasma albumin percentage after intravenous albumin therapy for periods varying from two to five weeks (See Table I). These observations are in accord with those of Thorn and associates[6] and Janeway and associates[7] who found that large amounts of albumin had to be administered before any improvement was observed in children or in adults with nephrosis. They also found that when the albumin level in the plasma was temporarily raised by an injection of concentrated albumin, there was a corresponding increase in protein excretion. Our findings on the amount of protein excreted in the urine after albumin injections agree with their observations.

DISCUSSION

The results of the present study have confirmed the well-known observation of a very low concentration of plasma albumin in lipoid nephrosis. Also confirmed is the increase in the concentrations of plasma globulin above normal limits as reported by Gottfried and associates,[12] Block and associates[13] and others. The increase in globulin concentration is both relative as shown by the increase in percentage distribution of the various globulin fractions and also absolute. Calculation of the grams of total globulin for eight of the nephrotic children studied from values for total protein obtained by chemical analysis gives values of 3.3 to 4.1 Gm. globulin per 100 ml. plasma. These values are much higher than the accepted normal range of 1.2 to 2.5 Gm. per 100 ml. The α_2- and β-globulin fractions seem to show the greatest increase but α_1-globulin may also be increased. Frequently if α_1 is high, β is not elevated markedly above normal. The reason for this apparent reciprocal relationship is not understood.

Possible explanations for the changes in globulin fractions observed in lipoid nephrosis can be postulated. As the albumin content of the plasma decreases either from decreased production, increased excretion, or a combination of these causes, the globulin components account for an increasingly higher percentage of the total plasma proteins. Globulins, having larger molecules, are not excreted so rapidly nor to so great an extent as albumin, therefore

favoring their relative increase in the plasma. The fact that α_2- and β- and, many times, α_1-globulins are increased disproportionately over fibrinogen and γ-globulin may be explained by the increase in the lipoprotein fraction in the plasma of nephrotic children. The lipoprotein fraction is usually associated with α_2- and β-globulins and would be reflected in the area of these components when a plasma containing the lipoid material was subjected to electrophoretic analysis. Since antibodies are known to be included in the γ-globulin fractions, the lower than normal concentration of γ-globulin in these nephrotic patients may explain the well-recognized susceptibility of these children to intercurrent infections.

Administration of concentrated salt-poor human serum albumin to children with nephrosis produced no striking changes in plasma protein distribution. Short periods of albumin administration of one to three days produced no change in the concentration of plasma albumin, confirming the findings of others.[5, 6, 7] Daily administration of 25 Gm. of albumin for periods of two to six weeks or longer usually brought about a moderate increase in the percentage of albumin, a decrease in the percentage of α_1-globulin, and often a decrease in β-globulin. In no case did concentration of plasma albumin, expressed as percentage of total protein or as grams per 100 ml., reach normal values. The administration of concentrated serum albumin to these children with lipoid nephrosis proved to be an effective diuretic but the marked diuresis, disappearance of edema, and resultant loss of weight were soon nullified by reaccumulation of edema fluid after termination of daily albumin administration. The clinical significance of these findings will be discussed in detail, together with our conclusions as to therapeutic value of salt-poor albumin in lipoid nephrosis, in a later paper.[14]

SUMMARY

1. Electrophoretic analyses have been made of plasma samples from eleven children with lipoid nephrosis. Distribution of the plasma protein fractions was determined in various stages of the disease and after intravenous administration of concentrated human serum albumin for periods of one to sixty days.

2. In general, the following changes from the normal percentage distribution of plasma proteins were noted in nephrosis: (a) a decrease in albumin, varying with the severity and duration of the disease; (b) an increase in α_2- and β-globulins and fibrinogen; (c) often an increase in α_1-globulin; (d) a decrease in γ-globulin.

3. Administration of concentrated serum albumin daily for long periods resulted in some cases in an increase in albumin, and usually a decrease in β-, α_2- and sometimes α_1-globulin concentrations. However, the changes were not maintained after albumin therapy was discontinued.

4. In nephrosis the urine may contain all of the protein fractions present in plasma except fibrinogen. Administration of concentrated human serum albumin intravenously results in an increase primarily in albumin excretion, although minor changes in the excretion of the globulin fractions may occur.

Ascitic and pleural fluids from children with nephrosis have a slightly different distribution of protein fractions than plasma samples from the same children.

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THE LET-DOWN REFLEX IN HUMAN LACTATION

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THE distinction between the secretion and the ejection of milk was first pointed out by Gaines.[1] The secreting animal must actively expel the milk; this is shown by the fact that the milk which is known to be present in the gland is only partly available to ordinary milking manipulations in anesthetized,[1, 2] or distracted animals,[3] or in udders which were excised and perfused,[4] or amputated at slaughter.[5, 6]

The mechanism by which milk is made available has been variously described as let-down (cows), draught (women), or the ejection, expulsion, or pumping reflex. It has been extensively investigated in domestic animals but few details are available as to its nature in the human species.

Let-down has been shown to be a reflex process, and, as a result of considerable investigation, Ely and Petersen[3] postulate the following mechanism: Nerves in the teat are stimulated by sucking or milking; impulses which cause the release of the oxytocic principle of the posterior pituitary gland are carried to the central nervous system. This substance reaches the breast by the blood stream and causes contraction of the smooth muscle surrounding the alveoli. Thus the contents of the alveoli are forced into the large ducts where they are available to the young or to the milking machine. In addition to the direct stimulus of sucking, psychic factors such as preparations for milking may initiate the reflex.

There is some evidence that a let-down reflex occurs in women.[7, 8] If a baby pulls away from a full breast for a moment, the milk may sometimes be seen to spray out of its own accord for a distance of several inches. Some women report subjective sensations during let-down, and milk may be observed to drip from the breast opposite that being sucked. It seems reasonable to suppose that the same mechanism occurs in women as in animals, and this investigation represents a preliminary attempt to test the correctness of Petersen's theory on a lactating woman.

METHODS AND RESULTS

The physical and psychologic difficulties of performing experiments on human lactation are many. It is for this reason that we feel justified in presenting the results of well-controlled studies on one subject.

The subject was a 25-year-old woman who was in good health. She had already successfully breast-fed one baby for eleven months. Her second child was a healthy, full-term girl weighing 7 pounds, 8 ounces at birth. She was entirely breast-fed on a self-demand schedule from birth. At the beginning of the study she was 7 months old, in good health, and weighed 19½ pounds. She was taking four to five breast feedings a day with a daily supplement of solid food and orange juice (about 250 calories). Both mother and child were well throughout the period of study.

The major part of the investigation was designed to show if the let-down reflex can be inhibited by distraction of the mother, and if a normal yield of milk can be obtained by combining a distraction with an injection of the oxytocic principle of the posterior pituitary gland.

It was established by preliminary experiments that the baby would take a relatively constant amount of milk at the first feeding in the morning under the following standard conditions: (1) the mother was basal; (2) only the right breast was used; (3) nursing time was limited to ten minutes; (4) the baby had not been fed for at least ten hours previously; (5) the baby had been awake for at least forty-five minutes, since it was found that she did not become hungry before that time; (6) every attempt was made to prevent the baby from crying before she was taken in to nurse, since crying produced premature let-down; (7) the baby was weighed before and after nursing, the difference in weight being the amount of milk taken. The scales were marked to measure to within ¼ oz. and with practice weights could be gauged to within ⅛ oz. (3.5 Gm.). The amount of milk taken was recorded to the nearest gram. All these conditions were fulfilled in every experiment. The fact that a consistent amount of milk was taken under these circumstances is shown by the mean figure of 194 Gm. of milk taken in fifteen preliminary experiments with a range of 177 to 219 Gm. and a standard deviation of 11 Gm.

Three types of experiment were performed: controls, distraction plus injection of saline, and distraction plus injection of Pitocin.* On control mornings mother and baby were not disturbed during the ten-minute nursing period. On distraction mornings a distraction was started about four minutes before the baby was due to be brought in. Two minutes later an injection of 0.3 c.c. of either Pitocin or sterile saline was given intramuscularly. The distraction was continued until the baby was brought in, and throughout the nursing period. The subject was not told beforehand whether the injection was to be of Pitocin or saline. The dose of Pitocin was determined after trials; an effect was produced by as little as 0.1 c.c., while 0.3 c.c. consistently produced a sensation of let-down in thirty to ninety seconds which was stronger than that produced by the baby sucking. No ill effects were observed in mother or baby from this dose of Pitocin.

The nature of the distraction to be used presented some problems, since distraction of the baby from sucking was undesirable; also, the mother was not easily prevented from letting down her milk and tended to become accustomed to any particular distraction if used on two or more successive days. It was finally decided to use three distractions. These were: (1) immersion of the feet alternately for ten seconds out of every thirty in ice water (The subject stated that this was the worst distraction.); (2) a combination of electric shocks of moderate intensity with a rapid series of questions involving mathematical problems (The shock was given when an incorrect answer was returned or the subject delayed more than ten seconds before replying. This distraction was effective in disturbing the subject emotionally and making her angry, although the

*Parke, Davis & Company posterior pituitary preparation containing 10 units of oxytocic substance per cubic centimeter.

effect was diminished when the baby was seeking food at her breast. It was noted that she then tended to have difficulty hearing the questions and frequently delayed answering.); (3) a length of surgical bandage was attached to each of the subject's big toes and pulled intermittently, causing sharp pain from the stretching and the tightness of the gauze around the toe.

The results of these experiments are shown in Table I. The mean amount of milk taken by the baby on distraction-plus-saline days is significantly lower than that taken on control days and significantly lower than that taken on distraction-plus-Pitocin days. The amount taken on distraction-plus-Pitocin days is lower, but not significantly so, than that taken on control days.* This eliminates the possibility of significant distraction of the baby, although it is likely that she was slightly affected by the proceedings. In the case of each individual distraction, the figures for the distraction plus Pitocin are higher than those for distraction plus saline.

TABLE I. EFFECT OF DISTRACTIONS, AND DISTRACTIONS PLUS INJECTION OF 0.3 C.C. PITOCIN ON AMOUNT OF MILK TAKEN BY BABY IN TEN MINUTES

CONTROL		DISTRACTION PLUS SALINE			DISTRACTION PLUS PITOCIN		
DATE	GM. MILK TAKEN	DATE	TYPE OF DISTRACTION	GM. MILK TAKEN	DATE	TYPE OF DISTRACTION	GM. MILK TAKEN
5- 1	153	4-29	TP	96	5- 7	TP	146
5- 2	177	5-20	TP	134	5-11	TP	170
5- 5	163						
5- 9	181	5- 4	IW	64	4-30	IW	127
5-12	142	5-15	IW	71	5- 8	IW	149
5-14	163						
5-19	209	5- 6	ED	113	5- 3	ED	174
5-21	153	5-10	ED	113	5-16	ED	156
Means	168			99			153

TP = Toe Pulling.
IW = Ice Water.
ED = Emotional Disturbance.

The second series of experiments were designed to illustrate the existence of the let-down reflex in a different manner. The left breast which was producing comparatively little milk was pumped by means of an electric breast pump at the same intermittent suction pressure for ten minutes either four or eight hours after it had been emptied by either the baby or the pump. One minute later the baby was put to the right breast. After the baby had sucked for one minute the breast pump was reattached and the left breast pumped for a further five minutes. In control experiments a two-minute interval was inserted between the two periods of pumping and the baby was not put to the right breast.

The results of these experiments are shown in Table II. Although the number of experiments is small, it will be seen that in each case, when the baby was applied to the right breast between the periods of pumping, the yield of milk in the last five minutes was much greater than that in the first ten minutes. In the control experiments it was less. It was noted that at no time did the mother feel a sensation of let-down to the breast pump alone, but a definite

*In these experiments a difference is considered significant if the possibility of the same or a greater difference occurring by chance is less than one in 100 ($p = 0.01$ using Student's t for calculation of the differences between means in small samples).

sensation of let-down was felt about sixty seconds after the baby began to suck vigorously. The fact that the mother did not let down to the breast pump is, perhaps, not surprising in view of the finding that wild animals who have been accustomed to suckling their young will let down their milk only with great difficulty to milking manipulations.[9]

TABLE II. EFFECT OF APPLYING BABY TO RIGHT BREAST ON YIELD OF MILK FROM LEFT BREAST TO A BREAST PUMP

DATE	HOURS SINCE LEFT BREAST EMPTIED	YIELD OF MILK IN CUBIC CENTIMETERS	
		0-10 MINUTES	12-17 MINUTES
(a) Baby on Opposite Breast			
5-13	8	3	11
5-16	3½	7	19
5-16	5	2	8
5-20	3	7	21
5-24	3½	2	7
Means		4	13
(b) Controls			
5-14	8	7	1
5-17	4	8	2
5-18	4½	4	2
Means		6	2

The third series of experiments was designed to show whether the effect of putting the baby to the breast could be duplicated by injections of Pitocin. All experiments in this series were performed at about the same time of day. The left breast was pumped for ten minutes approximately eight hours after the baby had last nursed at it. The same breast pump and suction pressure were used as in the second series of experiments. One minute later Pitocin (0.3 c.c.) was injected intramuscularly. After waiting one minute, pumping was again performed for five minutes. On control days 0.3 c.c. of sterile saline was injected instead of the Pitocin. The subject was not informed of the nature of the injection.

TABLE III. EFFECT OF INJECTION OF 0.3 C.C. PITOCIN ON YIELD OF LEFT BREAST TO BREAST PUMP

DATE	HOURS SINCE LEFT BREAST EMPTIED	YIELD IN CUBIC CENTIMETERS	
		0-10 MINUTES	12-17 MINUTES
(a) Pitocin			
4-26	8	11	26
4-29	7	9	20
4-30	7	9	27
Means		10	24
(b) Control			
4-28	7½	8	2
5- 2	8½	10	4
5- 6	8½	11	4
Means		10	3

The results of these experiments are given in Table III. The amount of milk produced during the first ten minutes was very constant in all experiments. However, Pitocin produced eight times as much milk in the second period as did saline. Pitocin injections were always followed in from thirty to ninety seconds by a subjective sensation of let-down which was more pronounced than

the normal let-down to the baby. Drops of milk appeared at that time on the nipple of the right breast which was not being pumped. It may be noted that the yield obtained after Pitocin was somewhat higher than that obtained after placing the baby on the other breast.

DISCUSSION

Inhibition of the central part of the let-down reflex has been produced in cows by Ely and Petersen.[3] Animals who were frightened or emotionally disturbed did not let down their milk. Our experiments show that a similar central inhibition can be produced in woman. Severe cold, emotional conflict (electric shock experiment), and pain significantly decreased the yield of milk. Inhibition is typical of a reflex mechanism. In other experiments not reported in detail the inhibition was at least partially overcome by the subject's taking a small amount of alcohol forty-five minutes previously. In two experiments the mean yield of the left breast to the breast pump in ten minutes was increased from a control figure of 10 c.c. to 21 c.c. In two other experiments of the same type the inhibition was restored in spite of the alcohol due to anger and embarrassment on the part of the subject; in these instances the mean yield was reduced to 6 c.c., or below the control figure.

It has been clearly shown that the efferent pathway of the let-down reflex is hormonal rather than nervous. Ely and Petersen[3] divided two out of three nerves to one side of the udder in three cows and showed that the yield was equal to that on the intact side. Petersen and Ludwick[4] showed that blood taken from a cow who had been stimulated to let down her milk would produce let-down when perfused through an isolated cow's udder, while blood taken from a cow not stimulated to let down had no effect.

It seems probable that the hormone responsible for the effect of the let-down reflex is produced by the posterior pituitary gland. The part played by this gland was first noted by Ott and Scott,[10] who found that injections of whole posterior pituitary extract greatly increased milk flow over a short period of time in a goat. This was confirmed by Mackenzie in cats,[11] Schafer in women,[12] Turner and Slaughter in cows,[13] and others. Gomez[14, 15] more definitely identified the action of the posterior pituitary. In hypophysectomized rats in whom milk secretion was maintained by injections of anterior pituitary lactogenic hormone and adrenal cortical hormone, the young failed to obtain milk although they sucked vigorously. With the addition of injections of posterior pituitary extract the young were able to obtain milk and thus survived. The observation by Smith[16] and Houssay[17] that successful lactation can occur after removal of the posterior pituitary is difficult to reconcile with this. However, it is possible that posterior pituitary hormones may be formed elsewhere than actually in the gland.

It is not certain exactly which posterior pituitary hormone is responsible for the effects. Ely and Petersen[3] found that normal let-down could be produced by injections of either the oxytocic or the pressor factor in distracted cows, but that in small doses the oxytocic factor was more effective. Petersen[18] showed the oxytocic principle to be effective in isolated, perfused udders. Our

experiments show that the oxytocic principle (Pitocin) has a similar effect on let-down in woman. Distraction plus Pitocin produced a normal yield, while in the breast pump experiments Pitocin produced an increase in milk flow similar to that produced by the application of the baby to the other breast. Turner and Cooper[19] showed that the pressor factor had some activity in causing let-down in the lactating rabbit. They suggested that possibly an unknown substance present in both pressor and oxytocic factors may be concerned. Petersen[18] tried the effect of various substances on let-down in isolated perfused udders and found that complete let-down was produced by Pitocin and acetylcholine, and that partial let-down was produced by Pitressin (pressor factor), epinephrine, histamine and acetyl-β-methylcholine.

It is not certain how the posterior pituitary hormone acts on the mammary gland. The most likely explanation is that it causes contraction of the smooth muscle fibers surrounding the alveoli. This was first suggested by Gaines,[1] using whole posterior pituitary extracts, and has been more recently advocated by Ely and Petersen,[3] using the oxytocic principle. This latter substance is known to cause contraction of smooth muscle elsewhere in the body, especially in the uterus, and its action on the breast would not be unexpected. However, there is considerable doubt about the existence of muscle fibers around the alveoli in animals, although Swanson and Turner[20] report finding them in the gland of a lactating cow. Muscle fibers have not been demonstrated in the human breast. Some additional evidence that the contents of the alveoli are actually forced out during let-down in woman is advanced by Waller[8] on the basis of fractional milking studies. He found that the hind-milk contained more fat than the fore-milk, which suggested a rapid forcing of milk and fat from the alveoli through the duct system.

Our results support the idea that Petersen's theory of the mechanism of let-down in animals holds for the lactating woman. It is interesting to speculate on the possible application of this knowledge to breast feeding in general. Many mothers are nervous about feeding their first baby; they are upset by the strange hospital surroundings; they are embarrassed by having to expose their breasts among strangers; their nipples are often sore and their breasts engorged. Emotional disturbances, embarrassment, and pain inhibit let-down to the sucking baby, and thus the baby gets little milk.

Furthermore, sucking itself is the primary stimulus which sets off the let-down reflex. Babies, brought to their mothers at scheduled times, may be so worn out with crying or so sleepy that they probably do not suck as vigorously as if they were applied when they woke up spontaneously and first sought food.

A vicious cycle is thus set up. Absence of let-down leads to more engorgement and more engorgement makes it all the more difficult for the baby to suck. Experiments by Gunther[21] on the effect of sucking show that when a baby sucks without getting milk for periods of over two minutes, characteristic erosive or petechial lesions of the nipple are produced. The mother often states that it feels as if the baby is biting her. In our experiments it was noted that when the baby sucked for prolonged periods without getting much milk (as in the ice-water distraction experiments) the mother's nipples were sore for some time afterward. It is likely that lesions of the nipple so produced may eventually

lead to complications such as breast infections and breast abscesses. Such misfortunes might well be averted by the administration of Pitocin and emptying the engorged breast by a breast pump or a hungry baby.

SUMMARY

1. The mechanism of the let-down reflex in human lactation has been studied.

2. The reflex can be inhibited centrally by distractions which affect the mother and not the baby.

3. This inhibition can be overcome by the intramuscular injection of Pitocin (posterior pituitary extract).

4. Application of a baby to one breast produces a great increase in the flow of milk from the other breast.

5. Intramuscular injection of Pitocin produces an increase in the flow of milk similar to and accompanied by the same subjective sensations as those produced by applying the baby to the other breast.

6. The significance of these findings in relation to breast feeding as a whole is discussed.

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OLLIER'S DYSCHONDROPLASIA

First Lieutenant Thomas G. Potterfield, Medical Corps, Army of the United States, and Major Juan Gonzalez, Medical Corps, Army of the United States

OLLIER'S disease is a developmental abnormality affecting the growing ends of long bones. It is characterized by malformation of the ends of the shafts, consisting of masses of unossified cartilage in the diaphyses. In most cases the condition is present in only one extremity or in both extremities of the same side of the body. It may affect the long bones of the hands and feet. This case is reported to demonstrate (1) the unilateral feature of the disease, (2) the x-ray appearance of the lesions.

CASE REPORT

The patient, a white female child aged 3 years, was admitted to the Fort Hamilton Station Hospital, March 30, 1948, with a chief complaint of "one hip higher than the other." One year previously it had been noted that the child limped slightly. The limp grew progressively more pronounced and the pelvis was tilted to the right at the time of admission. At birth it had been noted that the dorsum of the left hand was puffy in appearance. It was felt that the puffiness had increased markedly during the previous year. The history revealed no other abnormalities of birth or neonatal period. The child had an adequate diet and supplementary vitamin intake. The family history was noncontributory.

Physical examination showed a 3-year-old white female who was alert, cooperative, and in no distress. The positive findings were limited to the extremities. The dorsum of the left hand was puffy in appearance, nonpitting, and the transpalmar measurement was 5.5 cm. The right hand appeared to be normal, with a transpalmar measurement of 4.75 cm. The left leg measured 41.25 cm., the right leg 36.9 cm., from the anterior superior spine to the internal malleolus. In the erect position the left gluteal fold was higher than the right and there was an obvious tilt of the pelvis to the right. There were no palpable tumors in the extremities. The child walked with a moderate limp.

Laboratory findings were as follows: Urinalysis, negative; hemoglobin, 13.0 Gm.; red blood cells, 4,350,000; white blood cells, 10,400, neutrophiles 36, lymphocytes 58, monocytes 3, eosinophiles 3; throat culture, alpha streptococcus and neisseria; blood studies, Kahn negative, cholesterol 201.4 per cent, total proteins 7.20 Gm. per cent, albumin 4.31 Gm. per cent, globulin 2.89 Gm. per cent, phosphorus 4.0 mg. per cent, alkaline phosphatase 8.3 Bodansky units, calcium 10.1 mg. per cent.

X-ray Studies.—Considerable information was obtained from the radiographic examination. The outstanding roentgenologic findings consisted of unilateral bone changes, characterized by nonossified areas of rarefaction alternating with areas of normal ossification. This was most evident in the diaphyses of such long bones as the humerus, radius, femur, and tibia on the right side. Similar bone changes were also demonstrable in the scapula, os pubis, and first metatarsal and phalanges of the right foot. Worthy of note was the oblique and longitudinal arrangement of the lesions in relation to the shaft, as well as the occasional involvement of the epiphyses. The lesions are medullary as well as cortical. The roentgenologic picture is highly suggestive of a disturbance of the normal osteogenesis rather than a congenital anomaly. In this case no deformities of the bones were detected except

From the Fort Hamilton Station Hospital, New York, N. Y.

Fig. 1.—Right hip, showing bone defects of the upper portion of the right femur, including the neck and both trochanters. The absence of cortical ossification and changes in the bone texture are noted. Similar changes are also present in the right pubic bone. Pelvic tilt is secondary to shortening of the right lower extremity. The left hip appears to be normal.

for early widening and tortuosity of the metaphyseal portions of the femur and tibia. The soft tissue shadows show no atrophy or tumefaction. The corresponding structures of the left side are essentially normal.

The clinical picture of this patient remained essentially unchanged during her hospital stay.

DISCUSSION

In Ollier's disease the normal ossification of cartilage in the affected ends of the bones is retarded and the unossified cartilage remains in the diaphyses. Ossification is prevented by the lack of normal degeneration and calcification, though some calcification may occur in parts of the periphery but without the changes of normal enchondral ossification. The cartilage in the diaphyses generally proliferates normally, but may occasionally take on independent growth leading to the formation of huge tumors, and consequent deformities. Since

Fig. 2.

Fig. 3.

Fig. 2.—Right knee, showing longitudinal and oblique areas of rarefaction due to unossified cartilage; these areas are present in the distal end of the femur and proximal end of the tibia. Epiphyseal involvement is also apparent. Left knee shows normal bones.

Fig. 3.—Right ankle, showing similar changes of the tibial metaphysis and epiphysis. Widening and flaring of the involved portions are precursors to gradual bone deformities. The left ankle is normal.

the lesions are close to the epiphyses, the growth of the limb is usually affected and shortening of the extremity results. The tumors are not true neoplasms but are rather the results of disturbances of the physiologic process of bone growth. The retardation of growth of certain portions of bone with normal growth in adjacent portions results in deformity. In rare instances the lesions have become sarcomatous.

The condition may be associated with other developmental abnormalities. In the case reported here a lymphangioma was present in the left hand.

The onset of symptoms is gradual during the early years of life. An early sign is the limp which develops due to the shortening of the affected lower extremity. Tumor and/or deformity may be the first evidence of the disease. Pain is not associated with the lesions.

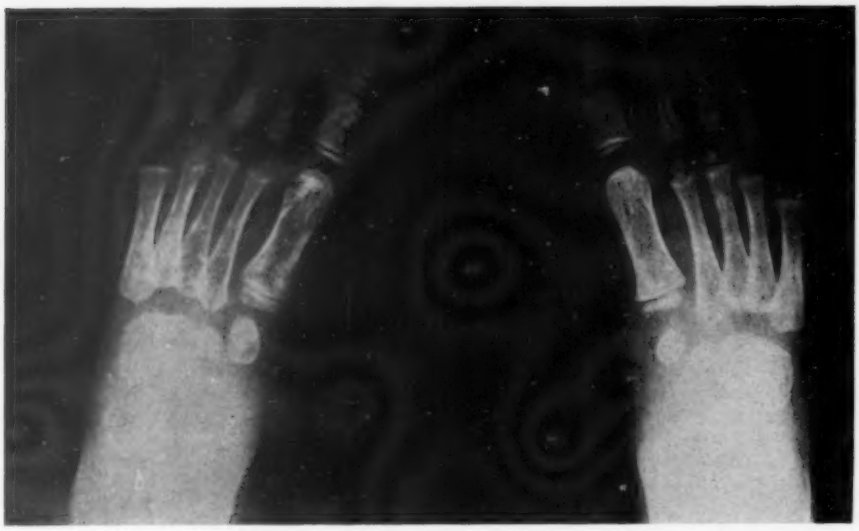

Fig. 4.—Right foot, showing minimal changes with irregularity, coarse trabeculation, and rarefaction in the metatarsals and phalanges of the big toes. The left foot is normal.

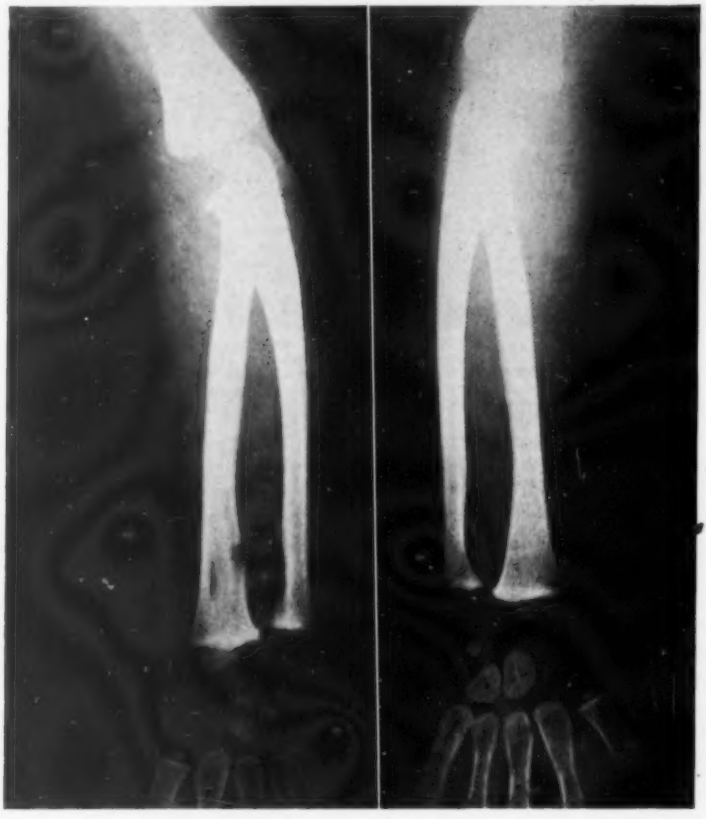

Fig. 5.—Right forearm, showing lesions in the right radius limited to the distal one-third of the shaft. Apparently normal ossification has been re-established in the growing portion of the bone. The left forearm is normal.

The diagnosis is established on the roentgenologic findings.

Treatment.—Orthopedic management for prevention or correction of secondary deformity is the only therapy of value.

SUMMARY

A case of Ollier's dyschondroplasia, involving the right scapula, humerus, radius, os pubis, femur, tibia, first metatarsal, and phalanges has been presented. The left side of the skeleton is not involved.

The disease is a developmental abnormality characterized by the presence of masses of unossified cartilage in the diaphysis of long bones. The lesions are generally unilateral in distribution.

The diagnosis is established on the roentgenologic findings.

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THE THERAPEUTIC USE OF PERITONEAL LAVAGE FOR ANURIA CAUSED BY TOXIC NEPHRITIS

Report of a Case

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SEVERAL papers have described the use of peritoneal lavage for the treatment of anuria resulting from such conditions as sulfonamide blockage, transfusion reactions, and mercury poisoning.[7-10, 12, 13] The purpose of this report is to emphasize the ease with which the procedure may be carried out and to describe its use in an additional case of toxic nephritis associated with pneumonia.

REPORT OF A CASE

M. H. was an 11-month-old white male infant admitted to Strong Memorial Hospital on Dec. 23, 1947, because of the sudden appearance of cyanosis and coma one hour before admission. He had a cough and nasal discharge for one week, and three days later developed wheezing respirations and fever. A physician prescribed Dover's powders to be given four times a day and advised the forcing of fluids. He improved and was free of wheezing until the evening of the fifth day of the disease, when wheezing began again and the temperature increased. Three days before admission he passed green, watery stools. Urination was normal. On the morning of admission, the patient's condition was unchanged. He retained his morning bottle feeding and moved about his crib. At 11 A.M. he was found unconscious, pale, and cyanotic, with rapid, panting respirations.

His mother had hypertension and edema during pregnancy. The infant, born two weeks after term, weighed 11 pounds. His development was normal. He received orange juice but no other vitamin supplements. He had no other serious infections previously, and had received no immunizations. There was no history of allergy. The family history was irrelevant.

Physical examination disclosed a well-developed, obese white male infant in a moribund state. The eyes were rolled up, the pupils were constricted. Respirations were deep, sighing, and regular, at the rate of 68 per minute. The blood pressure unfortunately was not recorded at any time during his hospital course. The skin was hot and dirty. Cyanosis was observed only in the nail beds. Both eardrums were injected but not bulging. The neck was supple. Over the right base posteriorly there were dullness to percussion, moist râles, and bronchial breath sounds. A to-and-fro friction rub was audible in the right axilla. Elsewhere, breath sounds were harsh with many audible rhonchi. The heart was not enlarged to percussion and no murmurs were audible, but the sounds were obscured by the noisy respirations. The liver was palpable 2 cm. below the right costal margin. No other organs were palpable.

On admission the red blood count was 3.5 million, the hemoglobin 11 Gm., and the white blood count was 51,000 with 57 per cent neutrophiles. The urine was normal although only about 5 c.c. was obtained. An x-ray of the chest revealed an acute pneumonic process in the right middle lobe and a suggestion of pneumonia in the left midlung field. The tuberculin skin test was negative. The nose and throat cultures grew pneumococcus Type 19. The serum carbon-dioxide combining power was 15 volumes per cent, the nonprotein nitrogen was 90 mg. per cent, the salicylate level was zero, and the icterus index was 7 units per 100 c.c.

Course.—Eighteen hours after admission the patient was still moribund although he had received the continuous administration of oxygen and of intravenous fluids, including 300 c.c. of M/6 sodium lactate and 200 c.c. of whole blood, and the injections of penicillin and sulfadiazine. He had passed only a few cubic centimeters of urine. By this time the non-

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protein nitrogen had risen to 127 mg. per cent. His condition seemed hopeless, for he did not respond to any stimuli and appeared to be in peripheral circulatory collapse. (Capsulotomy of the kidneys was considered but dismissed as it was felt that the procedure was too dangerous under the circumstances.) Diathermy to the kidneys and the intravenous injection of aminophylline failed to stimulate the secretion of urine.

At this point, peritoneal lavage was instituted using the technique of Bassett.[13] A No. 14 mushroom catheter was inserted into the right flank and a sump drain was introduced through a left flank incision by Dr. Paul Schloeb.

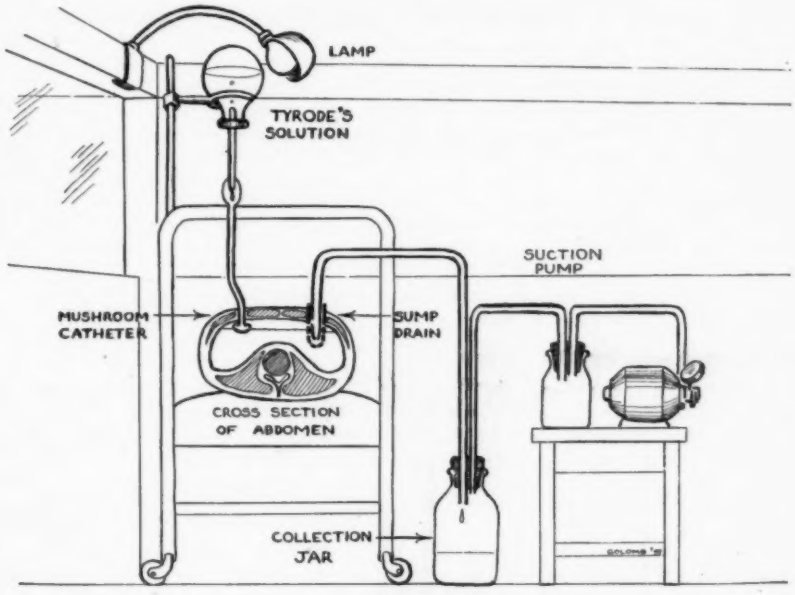


Fig. 1.

During a five-day period, 19,570 c.c. of solution was introduced and a total of 20,020 c.c. withdrawn. The solution used was a modified Tyrode's solution containing, per liter, the following:

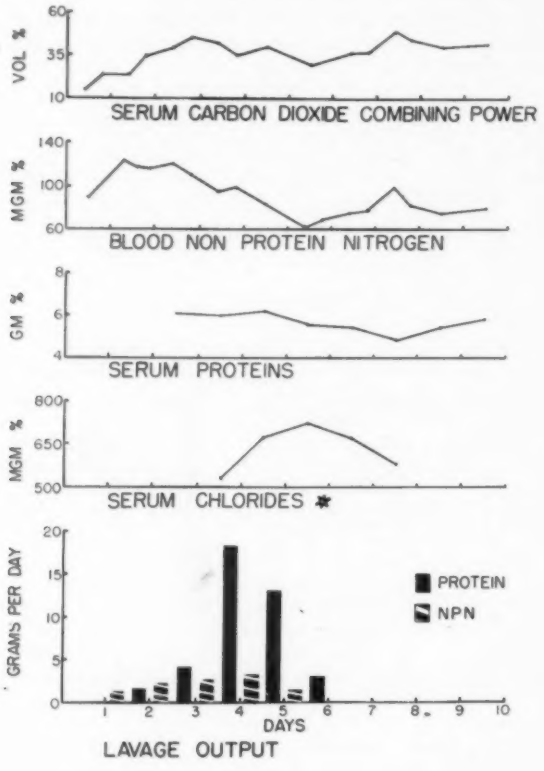
NaCl	9.0 Gm.
KCl	0.2 Gm.
$CaCl_2$	0.2 Gm.
$MgCl_2$	0.1 Gm.
NaH_2PO_4	0.05 Gm.
$NaHCO_3$	0.5 Gm.
Glucose	10-20 Gm.
Penicillin	100,000 units

The $NaHCO_3$, glucose, and penicillin were added after the autoclaving process.

The salts were calculated for 1,500 c.c. and were weighed in individual paper cups and added to six or eight flasks, each containing 1,500 c.c. distilled water. The flasks were then autoclaved and at least three were kept available for replacement when the previous flask was exhausted The calculated amounts of $NaHCO_3$, glucose, and penicillin were added to the solution just before it was to be used.

The apparatus (Fig. 1) included an inverted 1,500 c.c. flask attached to a Murphy drip apparatus and direct tubing from this to the mushroom catheter. The perfused fluid was

then withdrawn from the sump drain by continuous suction into a waste bottle. A gauge on the suction apparatus allowed for regulation of its suction pressure. A heat lamp focused on the solution in the flask kept it at approximately body temperature. The Murphy drip was adjusted to allow the solution to perfuse at the rate of 4 L. every twenty-four hours.



* expressed as NaCl

Fig. 2.

The patient received fluids, including whole blood and human serum albumin, by vein. It appeared unnecessary to add sodium and chloride ions, since these were probably adequately supplied by lavage. Vitamin B complex and ascorbic acid were also administered parenterally. In addition, he received oxygen continuously, Wangensteen suction to control abdominal distension, and 50,000 units of penicillin every three hours subcutaneously. Unfortunately, the amount of fluid withdrawn by Wangensteen suction was not recorded. After the first forty-eight hours the patient gradually improved, and by the fourth day was able to take fluids by mouth. He began to urinate by the third day and passed 30 c.c. of urine on the fourth day. The nonprotein nitrogen gradually dropped until it reached a level of 63 mg. per cent on the fourth day. On that day the Wangensteen suction and peritoneal lavage were clamped off and he continued to pass urine up to 32 c.c. The following day, the catheter and sump drain were removed and the sump wound was closed by one triple zero catgut suture. On the next day he seemed better and continued to pass urine. During the period when peritoneal lavage was operating, he passed no stools but passed one, five, and

six stools, respectively, on the first, second, and third postlavage days. The use of oxygen was discontinued on the second postlavage day. The nonprotein nitrogen rose following discontinuance of the lavage but fell again to 77 mg. per cent on the second postlavage day. Later that day a portion of bowel herniated through the sump drain incision. The hernia was reduced by operation and the wound reclosed. The next day the temperature rose to 40.8° C. Streptomycin therapy was begun. *Bacillus aerogenes* was cultured from the blood. The next morning he began to have rapid respirations and shortly thereafter was found dead.

AUTOPSY

(Performed by Dr. H. Tesluk on Jan. 2, 1948, approximately four hours after death.)

Gross.—

General: The pertinent findings were as follows: The peritoneum contained 150 c.c. of clear, yellow fluid. The omentum and a few loops of small bowel were adherent to the under-aspect of the sump drain incision and the peritoneum in this area was covered with granulation tissue showing brownish discoloration. Directly in the midline were several other loops of small bowel which were quite red and edematous and adherent to each other with fibrinous adhesions. Elsewhere there was no peritoneal reaction. There was 100 c.c. of clear, yellow fluid in the left pleural cavity. The right pleural cavity contained no excess of fluid but there were many delicate adhesions between the visceral and parietal pleura over the lower lobe of the lung. The pericardial cavity contained a few cubic centimeters of clear, yellow fluid.

Heart: The heart weighed 75 Gm. and was essentially normal in appearance.

Lungs: The left lung weighed 145 Gm., the right weighed 153 Gm. The left lung showed many small, firm, raised, dark areas of bronchopneumonia. In the upper lobe there were many discrete, white areas a few millimeters in diameter. The pleura of the right lower lobe was granular and many minute ecchymotic areas were scattered over the surface of the lung. The bronchi were edematous. Patches of slightly raised granular areas were seen on section of the middle lobe. The upper lobe showed areas of meaty, airless tissue and several firm, yellow, discrete areas varying from a few millimeters to 1.5 cm. None of them was liquid.

Spleen: The spleen weighed 95 Gm. and was firmer than normal. Prominent malpighian corpuscles were noted.

Gastrointestinal tract: The localized peritoneal reactions of the small bowel have been described. One of these involved about 4 cm. of small bowel and was located in the mid-portion of the ileum. The other area was more extensive, involving 15 cm. of lower ileum. The mesentery of this portion was edematous, hemorrhagic, and covered with fibrin. The nodes were enlarged and soft.

Pancreas: Normal.

Liver: The liver weighed 670 Gm. and was normal except for some swelling and translucency of the parenchyma.

Adrenals: Normal.

Kidneys: The left weighed 123 Gm., the right weighed 115 Gm. The cortex was pale with many small, dilated vessels and a few minute, petechial hemorrhages. On cut section the pallor was striking, striations were faint, and glomeruli were made out with difficulty. No hemorrhages were seen internally. The mucosal lining of the calices and pelves was somewhat roughened and injected. There was some narrowing of the ureteropelvic junction of the left kidney but none of the right.

Pelvic organs: The bladder contained only a few cubic centimeters of rather cloudy urine. The mucosa was shiny and gray and the ureteral orifices were normal.

Brain: The brain weighed 1,050 Gm. There was slight edema and on section there was moderate injection of the vessels in the white matter.

Histological.—

Heart: Normal.

Lungs: One section showed multiple abscesses which were quite large and had necrotic, pale centers surrounded by a zone of neutrophiles, and this in turn by a zone of hemorrhage.

The bronchioles showed sloughing of the epithelium. Other areas showed finely granular exudate in the alveolar spaces. There were frequent areas of hemorrhage. The pleura showed a layer of fibrin on its surface. There was edema of the intima of the pulmonary arteries with inflammatory infiltration.

Spleen: The spleen showed a healing infarct and many neutrophiles in the pulp.

Gastrointestinal tract: Section of the small bowel involved in the evisceration showed injection, hemorrhage, and edema. Section of the left abdominal incision showed necrosis, edema, and granulation tissue involving skeletal muscle with sutures and foreign body reaction.

Adrenal: Edema and one small area of necrosis in the cortex were noted.

Kidneys: There was marked interstitial edema and frequent focal collections of round cells in the stroma. The edema seemed to involve loops of the glomerular tufts. Tubules in the cortex were dilated and lined by flattened, pale-staining epithelium which contained no fat. In a few areas epithelial cells had proliferated to form projections into the lumen.

Brain: This was normal except for the presence of clumps of bacteria in a few blood vessels.

Cultures: The post-mortem cultures of the lungs showed *B. aerogenes.*

The sections were reviewed by members of the Department of Pathology. They believe that the necrotizing pneumonia had been going on for some time and was the primary pathologic process responsible for death. The changes in the kidney were apparently secondary to the acute pulmonary infection and appeared to be a combination of acute interstitial nephritis and subsiding tubular degeneration.

COMMENT

A case of severe necrotizing pneumonia in an 11-month-old male infant complicated by toxic nephritis with anuria is described. Death resulted from septicemia caused by *B. aerogenes,* secondary to postoperative herniation of small bowel through the sump-pump incision. Whether or not he might have survived, had streptomycin been started immediately upon discovery of the herniation, is a matter of conjecture. Although the patient died, it is probable that the anuria associated with toxic nephritis was corrected by peritoneal lavage as indicated by the favorable clinical response, by the continued fall of the blood nonprotein nitrogen values after its institution, and by the evidence of healing tubular degeneration found at autopsy. As illustrated in the accompanying graph, the response of the nonprotein nitrogen to the procedure was both prompt and sustained. The same chart illustrates an astonishing loss of protein in the peritoneal lavage fluid. Although human serum albumin was supplied to replace the protein loss, it failed to completely compensate for the large loss resulting from lavage. An entirely satisfactory explanation of this loss of protein is not available. However, it is well known that the peritoneal surfaces of infants are permeable to protein molecules, an observation which has led to the use of intraperitoneal blood transfusions in them. Moreover, the gastrointestinal tract of infants is also known to be particularly permeable to protein molecules.

Another problem which arose in our study was the correction of acidosis which required the frequent parenteral administration of alkali. The blood chlorides rose to a high level during lavage, but returned to normal when the glucose concentration of the lavage fluid was adjusted to correct a moderate dehydration. The serum phosphorus values ranged between 3.9 and 5.0 mg. per cent, while those for calcium varied between 7.1 and 8.0 mg. per cent.

The history of the use of peritoneal lavage began many years ago. The earlier observers[1, 2, 3] used an injection-withdrawal technique with a time lag between injection and withdrawal. By this method, Bliss and co-workers[1] kept nephrectomized dogs alive for thirteen to sixteen days, compared with a survival time of two to three days for the untreated dogs. By the same method,[2] rabbits given bichloride of mercury showed a far greater recovery rate following peritoneal lavage. Rhodes[3] used this method in two human subjects. Although the patients failed to survive, they showed a temporary fall in blood urea nitrogen.

The first successful use of continuous lavage in man was by Wear.[4] He used two trocars, one a standard gall-bladder trocar in the upper abdomen, and the other a trocar with numerous perforations in its distal end to avoid occlusion by omentum and intestines. The perfusion fluid was Locke-Ringer's solution. One of the three patients on whom this method was used, survived. He had renal shutdown secondary to bladder calculi and benign prostatic hypertrophy.

The preferred type of fluid was discussed by Abbott and Shea.[5] They found that a perfusion solution with a chemical consistency closely similar to that of interstitial fluid was the most suitable for lavage.

Seligman, Frank, and Fine[6] were the first to use Tyrode's solution. They treated nephrectomized dogs and included penicillin, sodium sulfadiazine, and heparin in their therapy. They calculated the blood urea clearance by peritoneal lavage to 41 to 48 per cent of the average renal clearance. They found the efficiency of peritoneal dialysis of urea to be one-third to one-half that of glomerular filtration. This did not take into consideration tubular reabsorption of urea. As a result of the clinical use of their method[7, 8] one out of four patients survived.

The indication for peritoneal lavage is temporary anuria resulting from toxic nephritis, sulfonamide toxicity, transfusion reaction, heavy metal poisoning, and any other condition which causes temporary anuria. It is realized that considerable difficulty may arise in judging whether anuria in a given patient is temporary or permanent; and, if temporary, in deciding the proper time to start the procedure. At any rate, peritoneal lavage is a means of combating temporary anuria which successfully lowers the increasing level of nitrogenous waste products in the blood stream. The high mortality of the patients treated with this procedure in the past may have been related in part to the severity of their illness prior to its initiation.

In the future the technique of continuous peritoneal lavage should improve with experience. The use of the mushroom catheter and sump pump has been found by several observers[9, 11] to offer a greater advantage than that of the mushroom catheters alone or that of trocars. Using this technique we had no difficulty with blockage of flow from omentum or bowel as was experienced in the case discussed by Bloxsam and Powell.[12]

Although heparin may be indicated in certain instances, it was found unnecessary to use this anticoagulant in our case. It is also probable that streptomycin should be administered to combat infections caused by gram-negative organisms.

The procedure described here can be set up in any modern hospital with a minimum of effort. The insertion of the draining tubes can be done safely at the bedside under aseptic conditions. The prompt use of streptomycin in the event of postoperative bowel herniation is suggested.

CONCLUSIONS

1. A case of toxic nephritis with anuria treated by peritoneal dialysis is described.

2. The simplicity of the apparatus is emphasized and its more general use in similar cases of temporary renal shutdown is urged.

The author is indebted to Miss Elizabeth Day and to Mr. Fred Golomb who prepared the graph and diagram.

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TOPICAL AND PARENTERAL PENICILLIN THERAPY IN RITTER'S DISEASE

Report of Four Cases With Recovery

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FOR many years the entity known as "Ritter's Disease" has carried with it an extremely high mortality. Most authors report a rate of 48 to 52 per cent; some, however, report a rate as high as 76 per cent. Herein is reported a series of four consecutive patients treated with topical and parenteral penicillin with a resultant 100 per cent survival.

CASE REPORTS

Case 1.—O. W., a white male infant, was admitted to Children's Hospital at 9 days of age. He was the product of an eight-month pregnancy which was terminated by an eight-hour uncomplicated labor. There were no infections or illnesses during the pregnancy, the only maternal complication being varicose veins of the legs. Oxygen and resuscitation were necessary at birth because of temporary failure of spontaneous respirations. Circumcision was deferred because the baby failed to gain weight as well as expected. Upon discharge from the hospital five days after birth the parents noted the face to be red and sore; this they attributed to scratch marks. The rash was first noted about the angles of the mouth and soon spread over the remainder of the face. By the seventh day of life the entire body had become involved with marked redness and "peeling" associated with a "yellowish" staining of the baby's clothes. He had been breast fed until the day of admission, when blood came from the breast, prompting the mother to institute an evaporated milk formula.

The past and the family histories were entirely negative. There was no family history of syphilis nor was there a history of the use of strong cleansing or disinfecting agents or the use of any drugs by the mother or infant.

The physical examination disclosed a fairly well-developed 9-day-old white male infant with marked redness and severe desquamation of the skin of the entire body. Many areas were denuded and markedly inflamed. These were more marked over the face, neck, buttocks, scrotum, hips, ankles, feet, and upper and lower thirds of the trunk. The nose, mouth, and throat were mildly inflamed. Upon rubbing islands of apparently normal skin, the epidermis peeled away disclosing raw, inflamed derma (Nikolsky's sign). The lungs were clear to percussion and auscultation and respirations were sixteen per minute. The heart had a normal rhythm and rate and the remainder of the physical examination was essentially negative. The temperature on admission was 100° F. by rectum. A white blood count of 35,000 with 33 per cent eosinophiles was obtained on admission. A skin lesion culture on admission showed hemolytic *Staphylococcus albus* and a skin lesion smear at the same time showed many gram-positive diplococci and a few gram-negative bacilli.

Treatment consisted of the removal of all clothing from the infant, including the diapers, the placing of a heat cradle continuously over his body, and the administration of penicillin intramuscularly with an initial dose of 100,000 units followed by 50,000 units every three hours. Penicillin ointment was placed generously over the entire body every six hours. Supportive fluids and vitamins in large dosages were also used throughout the entire hospital stay. Intramuscular penicillin was continued for nine days and the ointment, heat cradle, and supportive measures for fifteen days.

From the Children's Hospital, Washington, D. C.

During the hospital stay there was increasing exfoliation with the fever reaching a peak of 101.2° F. on the second day. Later, as the erythema of the face began to subside, the desquamation progressed over the entire body. Four days after admission the patient appeared much improved with the exception of a few small areas of desquamation. By the ninth hospital day the skin appeared normal and the intramuscular penicillin was discontinued. On the fifteenth hospital day all other medications were discontinued and on the twenty-fourth day he was discharged, completely recovered.

CASE 2.—J. R., a white male infant, was admitted to Children's Hospital on the sixth day of life. He was the product of a full-term pregnancy, during the second month of which the mother had had pityriasis rosea. At the age of 3 days a scratch was noted on the baby's face and on the following day this scratch was surrounded by an erythematous rim. A generalized fine desquamation of the skin was also present. On the fifth day scaly and erythematous lesions were noted on the hands and forearms. These became larger and confluent and by the time of hospitalization had spread over most of the body surface.

The family history other than that mentioned previously was irrelevant. Syphilis was denied, as was the use of any drugs or harsh agents for cleansing or disinfection.

The physical examination revealed a well-proportioned newborn boy appearing moderately ill with marked erythema, scaling, and desquamation of the face and body being more marked in the axillary folds and folds of the thighs. The scalp contained a few areas of scaling. These areas contained vesicles and bullae with serous fluid as well as crusting patches. Nikolsky's sign was positive. The eyes, ears, and nose were normal and the throat was moderately injected. The remainder of the physical examination was negative. A hemogram was essentially normal, showing 8,900 leucocytes with 7 per cent eosinophiles. A blood culture showed hemolytic *Staph. aureus*. Kahn and Mazzini tests for syphilis were negative. The temperature was normal during the entire hospital stay.

Treatment consisted of 30,000 units of penicillin given intramuscularly every three hours and the application of penicillin ointment to the skin lesions. Two days after admission a heat cradle was utilized and the fluid intake increased. At that time daily administration of 100 mg. of vitamin C and one cubic centimeter of soluble vitamin B was begun. The penicillin ointment was discontinued on the fifth hospital day and the intramuscular penicillin and other medications were discontinued on the seventh hospital day.

The desquamation continued for four days, after which the erythema gradually diminished and re-epithelialization of the skin occurred. On the eighth day the patient was discharged in good condition.

CASE 3.—G. C., a white male infant, was admitted to Children's Hospital when 6 days of age. He was the product of a normal, full-term pregnancy and an uncomplicated labor. Two days prior to admission he developed a generalized erythematous rash, following a fine desquamation of the skin. The rash first appeared on the face and about the mouth and spread to the creases of the groin, axilla, and neck. The erythematous patches rapidly increased in size until the entire body was involved. One day before admission a mild diarrhea developed.

The past and family histories did not reveal the use of any drugs or cleansing agents nor was there a history of allergy, heart disease, skin disease, or venereal disease.

The physical examination disclosed a well-developed and -nourished newborn white male infant in no acute distress. The entire skin was markedly inflamed and exfoliation was noted on both cheeks and on the forehead. The patches of exfoliation measured up to 5 by 8 cm. in size. The outer layers of skin could be removed easily by gentle rubbing, leaving an underlying, raw, red derma resembling a second-degree burn. The exfoliations were most prominent in the right anterior cervical fold, left groin, and left popliteal space.

Treatment consisted of intramuscular penicillin, 30,000 units every three hours, and topical penicillin ointment applied every eight hours. In this case a protein milk formula was used on admission; however, this was soon replaced by evaporated milk. One cubic centimeter of vitamin B complex was given daily. The intramuscular penicillin was discontinued on the fifth hospital day and penicillin ointment on the seventh day.

Within a few days after admission the scaling had extended over the entire body, vesicles and bullae had appeared, and serous fluid was noted beneath the areas of desquamation. By the sixth day the skin was entirely denuded and new areas of normal skin had begun to appear. On the seventh hospital day all medication was stopped and on the tenth day the patient was discharged, the skin being entirely normal.

CASE 4.—S. M., a white female infant, was admitted to Children's Hospital when 3 weeks of age. She had been well until three days prior to admission when she developed "small white pimples" on her buttocks. On the following day a fine desquamation appeared in the same region and shortly thereafter this was noted on the neck, face, ears, and in the axillae. One day before admission a physician prescribed mineral oil and a "tar paste" preparation for application on the involved areas. She had been breast fed since birth and the mother had taken no drugs or medications for more than one year. Neither orange juice nor cod-liver oil had been a part of the infant's diet. The patient had been bathed exclusively in olive oil since birth with the exception of the mineral oil mentioned previously. No history of contact with cosmetics, new clothes, or other possible irritants could be elicited. She had been the product of a full-term, normal pregnancy followed by an uncomplicated labor and delivery. There were no neonatal complications. The family history was irrelevant. No history of venereal disease could be elicited.

The physical examination revealed a well-proportioned, restless white female infant with a generalized scaly rash over the face, neck, buttocks, and axillae. Discrete vesicles filled with clear fluid were noted over the skin of the face and scalp. Some of these had ruptured, leaving crusts, and many crusts were present in the creases of the neck and axillae. Erythematous, denuded, moist areas were noted on the buttocks. Nikolsky's sign was positive. The remainder of the physical examination was negative.

Penicillin ointment was applied generously to the entire body three times daily and intramuscular penicillin, 50,000 units every three hours, was also employed. Phenobarbital was used as needed to prevent scratching and restlessness. As with the other patients, all clothes were removed from the infant's body, mineral oil was used to remove crusts, and a heat cradle was placed over the baby. Nutramigen and a high vitamin diet were employed. On the thirteenth day all medication was discontinued.

A few days after admission other erythematous areas began vesiculating and four days later the skin began exfoliating from these areas leaving a denuded, inflamed derma. At that time the skin of the face began assuming a normal appearance and by the thirteenth day the entire body appeared normal. The patient was discharged on the seventeenth day.

DISCUSSION

Probably all forms of exfoliative dermatitis are merely reactions of the body to systemic or local irritants. Such irritants may be classified under the headings of living and nonliving, the living irritants including pathogenic microorganisms and animal parasites and the nonliving including physical (trauma, electricity, pressure, light, roentgen rays, radium radiations, foreign bodies, heat, cold, etc.) and chemical (drugs, poisons, acids, alkalis, etc.) agents.

The diagnostic terminology applied to each individual case of exfoliative dermatitis is generally determined by the irritant or irritants involved plus the clinical course of the disease and not by the skin lesions alone for several separate disease entities may exhibit almost identical skin lesions.

Ritter's disease (dermatitis exfoliativa neonatorum, keratolysis neonatorum) will be fully discussed, with the thought in mind that Leiner's disease, Savill's disease, pemphigus neonatorum, acute epidermolysis of the newborn, impetigo of the newborn, and possibly drug or contact dermatitis of the newborn are probably merely variants of this same condition, since the clinical pictures are quite similar.

The etiological agent responsible for Ritter's disease remains obscure, most authors favoring an infectious origin (staphylococcus, streptococcus, virus, etc.) while a few favor a disturbance of the endocrine system. In all probability the infectious nature is merely the result of secondary invaders or contaminants. It is our belief that the causative factor may be any type of irritant, either systemic or topical.

The onset of the condition known as Ritter's disease may occur from the second day of life to the fifth week, the average occurring during the second week. It may be sporadic or epidemic in nature, depending on the causative irritant involved. The disease usually runs its course in a period of seven to ten days; however, severe cases may last a month or longer. Recovery is usually permanent although recurrences are not too uncommon, some developing years after the initial attack.

The skin rash itself has been described in all gradations of severity and type, hence we will discuss the picture as it may occur, keeping in mind that all or any part of this picture may exist. The rash is generally preceded by a fine desquamation of the skin, and begins with erythematous patches which enlarge and coalesce. These patches progress to the point of exfoliation, leaving thin or thick scales of epidermis covering the body and overlying a raw, red derma appearing not unlike a second-degree burn. The derma beneath the crusted, exfoliated epidermis is generally moist although it may be dry and inflamed. Vesicles and bullae with inflamed areolae may be present, the vesicles having a tendency to confluency and the bullae containing serous or purulent fluid. These lesions also rupture and desquamate as previously described. Crust-covered fissures at the mucocutaneous junctions are not uncommon. Islands of apparently normal skin, when gently rubbed or traumatized, exhibit the phenomenon of epidermolysis; i.e., the epidermis peels away revealing a raw, inflamed, usually edematous derma (also known as Nikolsky's sign). With the cessation of the scaling there is a gradual diminution and clearing of the erythema and re-epithelialization of the skin.

The rash usually begins on the lower part of the face, i.e., the cheeks, chin, and angles of the mouth, and spreads rapidly to the neck, arms, legs, and body. Exfoliation is generally evident within one to three days of the onset. The mucous membrane of the mouth, nose, and conjunctiva may be involved and there may be edema of the eyelids, lips, ears, and legs.

The temperature is usually below normal or within normal limits; however, an occasional patient may run a fever as high as 104° F. and chills may occur.

The majority of deaths due to Ritter's disease are the result of complications, hence the major part of the treatment should be directed toward the prophylaxis against complications. We attribute the survival of our four patients largely to the prophylactic use of parenteral and topical (ointment) penicillin, thus preventing the complications that are usually considered to be the causes of death.

The uncomplicated case generally presents few or no constitutional symptoms whereas the complicated case usually exhibits symptoms referable to the gastrointestinal tract, such as vomiting, diarrhea, marasmus, etc. Following

are complications of Ritter's disease, extracted from the literature, that are thought to decrease the infants' chances of survival: pneumonia, furuncles, abscesses, stomach and intestinal ulcers, secondary infections, gangrene, sepsis, septicemia, dehydration and anuria, hypothermia, toxemia, hypoproteinemia, lymphangitis, lymphadenitis, Waterhouse-Friderichsen syndrome and other endocrine disturbances.

Many forms of treatment have been employed. Among the topical forms are ointments of sulfonamides (sulfanilamide, sulfathiazole), ammoniated mercury, zinc oxide, tar, Ichthyol, cold cream and chrysarobin; oils such as olive and carron; powders as talcum, zinc oxide, starch, and zinc peroxide; solutions of potassium permanganate, tannic acid, methylene blue and physiologic sodium chloride; and tincture of benzoin. Breast feeding has been considered a must and oral medications have consisted of sulfapyridine, sulfathiazole, sulfadiazine, sulfanilamide and vitamins A, C, D, and B. Transfusions of whole blood, intramuscular injection of human serum or maternal blood, ultraviolet radiation, and small doses of roentgen radiation have been employed.

In view of the excellent results obtained with the four cases herein reported, it appears as though the most satisfactory form of therapy to date consists of general maintenance, warmth (heat cradle), no clothes, no baths, as little handling as possible, and intramuscular penicillin and penicillin ointment applied topically (so that the entire body is covered and moist at all times). It is suggested that these measures be employed for several days after complete recovery in order to avoid the possibility of a recurrence. Sulfonamides may be employed if deemed necessary. Any mode of therapy must be directed toward the prevention of complications.

SUMMARY

1. Four patients with Ritter's disease have been treated with topical and parenteral penicillin with 100 per cent recovery.

2. It is believed that the results obtained were due to the prevention of complications.

3. The etiology, diagnosis, complications, and treatment of Ritter's disease are briefly discussed.

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TWO UNUSUAL VASCULAR AND CARDIAC ANOMALIES

I. Vascular Ring of the Esophagus and Trachea With Patent Ductus Arteriosus Origin of the Left Subclavian and Carotid Arteries

II. Persistent Atrioventricular Communis and Aortic Dextroposition With Mongolism

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ADDED interest in congenital vascular and cardiac anomalies has been aroused by recently developed methods for the surgical correction of some of these defects.[1, 2] The basis for these new methods has developed over many years through studies of the etiology, incidence, and diagnosis of the heart anomalies. When the post-mortem findings are correlated with the clinical symptoms and signs, the diagnosis and treatment of similar cases in the future will be made easier. These two congenital anomalies are reported with this objective.

Case 1.—This full-term, white, male infant was delivered at St. Luke's Hospital on March 2, 1948, in the service of Dr. J. E. Fitzgerald. Death occurred approximately thirty hours later.

History.—The mother was a 20-year-old gravida ii, para i, white woman. Her prenatal condition had been uneventful. She had gained twenty-six pounds in weight, and gave no history of having contracted any infectious or contagious diseases during pregnancy. She entered the hospital in active labor on March 2, 1948, at 5:30 A.M., and after one hour spontaneously delivered a full-term living male infant weighing 5 pounds, 14½ ounces. Respirations began at once and the cry was described as fair in quality. The infant had bilateral congenital absence of the lobule and the inferior portion of the helix of the ears, and the testicles were not palpable in the scrotal sac.

He was transferred to an oxygen-tent-crib in the nursery because of slightly labored respirations and excessive mucus exuding from the nasal passages. Frequent nasopharyngeal aspirations were necessary because of the copious quantities of mucus which continually accumulated and exuded from the nose and mouth. Cyanosis of the skin of the face, especially about the nose and mouth, appeared but improved markedly following the nasopharyngeal aspirations. Twelve hours after delivery an unsuccessful attempt was made to give water by mouth, and body fluids were maintained by subcutaneous injections of Ringer's lactate solution. On the second day after birth the rectal temperature was 100° F. A loud systolic murmur was heard over the entire precordium, the breath sounds in the left chest were decreased, the respirations were labored, mucus secretions in abundance continued to exude from the nose and mouth, and cyanosis of the skin of the face persisted despite the continuous administration of oxygen and frequent nasopharyngeal aspirations. Penicillin and Synkamin were given but he failed rapidly and expired approximately thirty hours after birth.

Excerpts from the necropsy protocol follow:

The body of this full-term, white male infant weighed 5 pounds, 14½ ounces, and had a crown-heel length of 47 cm., a crown-rump length of 34 cm., a congenital absence of the lobule and the inferior portion of the helix of the ears, and no palpable testes in the scrotal sac. When the chest structures were exposed several anomalies of the main cardiac vessels

From the Henry Baird Favill Laboratory, St. Luke's Hospital.

were observed (Figs. 1 to 4). These are listed as follows: (1) persistent aortic right arch and congenitally absent aortic left arch; (2) patent ductus arteriosus from which ascended the left common carotid artery and the left subclavian artery; (3) dilatation of the pulmonary conus; (4) congenitally absent innominate artery; (5) persistent left superior vena cava, which emptied into the right auricle of the heart, and communicated with the right superior vena cava through the left innominate vein.

The aortic right arch arose at the base of the heart, ascended, and curved in front of the right main bronchus. The arch then extended posteriorly behind the esophagus and trachea and emerged to the left and posterolateral side of these structures. At this level the aortic arch was joined by the ductus arteriosus and thus formed a vascular ring about the trachea and esophagus. The left common carotid artery and the left subclavian artery arose from the ductus arteriosus. After the aortic arch had anastomosed with the ductus arteriosus, the aorta descended as usual on the left side.

The myocardium of the heart was dark red-brown, fibrillar tissue. No unusual changes were in the right and left lungs, main bronchi, or trachea. The lining of the urinary bladder was gray and the lumen was markedly dilated. The urethra and uretheral orifices were patent. The prostate gland was 1 by 1.2 by 0.6 cm. and surfaces made by cutting were gray, fibrillar tissue. The verumontanum was enlarged to 0.5 by 0.3 by 0.4 cm., and appeared partially to obstruct the urethral meatus. No other significant changes were observed on gross examination of the remaining tissues of the body.

Histologic examination of the tissues stained routinely with eosin and hematoxylin revealed: hyperemia and moderate atelectasis of the lungs; hyperemia and fatty changes of the liver; hyperemia of the spleen; and extramedullary hematopoiesis of the liver and spleen.

DISCUSSION

In reviewing the development and modification of the aortic arches and the normal embryology of the vascular system, Congdon's[3] excellent monogram and various embryologic texts[4, 5] have been consulted. In the human embryo, six pairs of aortic arches develop, all of which are not present at any one time during fetal development. The period of development of the aortic arches extends throughout the fourth week, and their transformation occupies mainly the fifth to seventh weeks. According to Arey, the characteristic changes of this region are brought about by the loss or interruption of some arches and segments of the aorta.

In the second week of embryonic life, the heart is a single chamber, on each side of which is a ventral aorta, an aortic arch, and a dorsal aorta. Toward the end of the fourth week the paired ventral aortas unite to form the bulbus arteriosus and the dorsal aortas combine to form a common descending aorta. Before fusion of the two dorsal segments, each gives off approximately thirty dorsal branches. After the fusion of the dorsal aortas these dorsal branches become the posterior paired intersegmental arteries.

The development of the six pairs of aortic arches occurs by the fusion of the dorsally growing branches from the bulbus arteriosus with ventrally growing branches from the dorsal aortas.

Normally the external carotid arteries represent the surviving elements of the paired ventral aortas. The internal carotid arteries are derived from the third arches and the persisting cephalic portions of the original paired dorsal aortas. The portions of the dorsal aortas which lie between the third and fourth arches disappear.

The proximal portion of the right ventral aorta becomes the right innominate artery. The right subclavian artery is derived from the fourth right arch, a persisting segment of the right dorsal aorta and the sixth intercostal artery. The sixth intersegmental arteries are usually incorporated in the subclavian arteries of both sides.

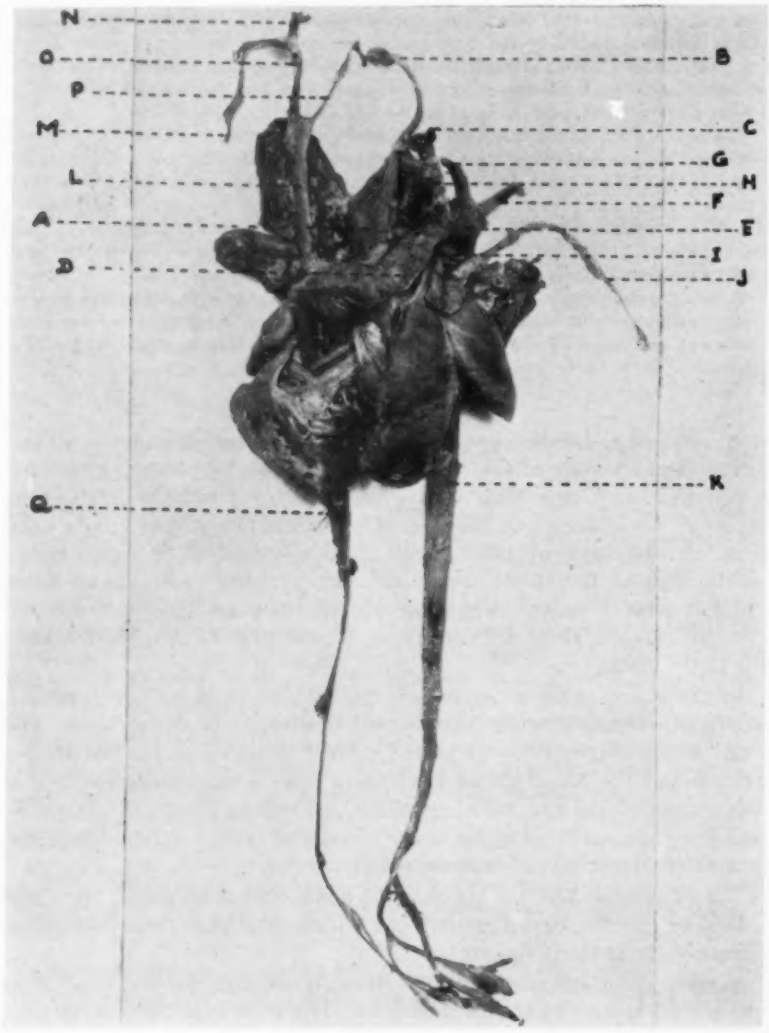

Fig. 1.—Ventral view of the heart and vascular tree illustrating *A*, aortic right arch; *B*, right subclavian artery; *C*, right common carotid artery; *D*, dilated pulmonary conus; *E*, ductus arteriosus; *F*, left common carotid artery; *G*, left subclavian artery; *H*, trachea; *I*, left pulmonary artery; *J*, persistent left superior vena cava; *K*, descending aorta; *L*, right superior vena cava; *M*, right subclavian vein; *N*, right jugular vein; *O*, right innominate vein; *P*, left innominate vein; *Q*, inferior vena cava.

On the left, the fourth left arch becomes the definitive aortic arch which continues caudally as the descending aorta.

The pulmonary arteries arise from the proximal portion of the sixth arches. Only on the left does the distal half of the sixth arch persist, and here it becomes the ductus arteriosus. When the bulbus arteriosus divides sagittally, the pulmonic and aortic systems become separate.

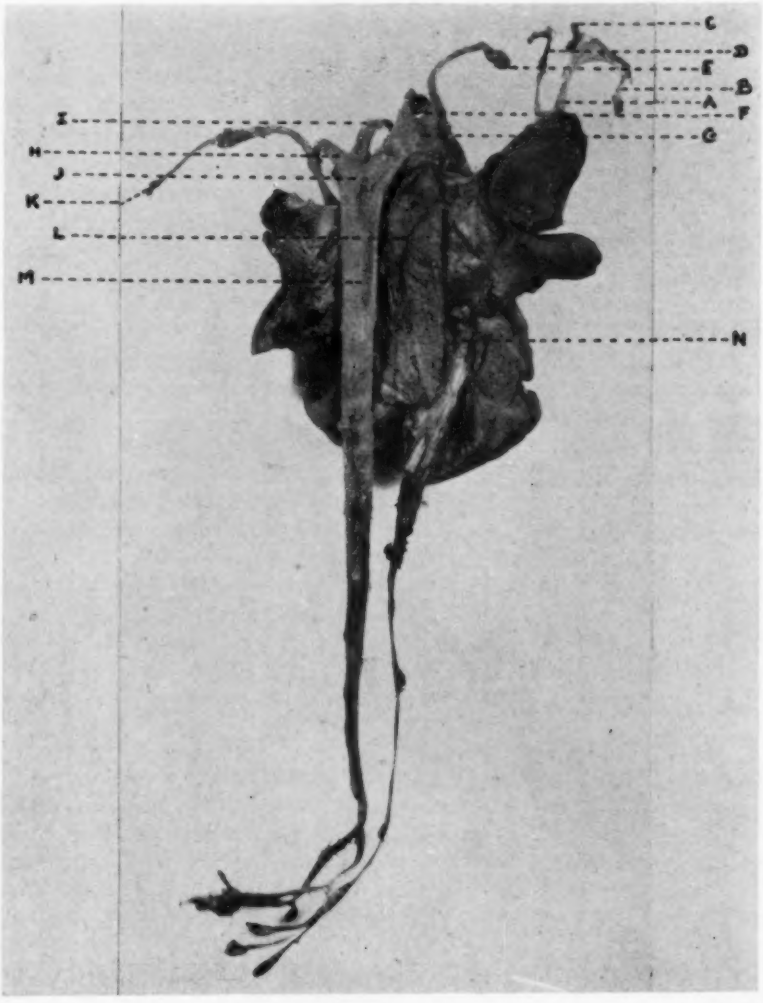

Fig. 2.—Dorsal view of the heart and vascular tree illustrating *A*, right innominate vein; *B*, right subclavian vein; *C*, right jugular vein; *D*, left innominate vein; *E*, right subclavian artery; *F*, right common carotid artery; *G*, aortic right arch; *H*, left common carotid artery; *I*, left subclavian artery; *J*, anastomosis of the ductus arteriosus with the aortic right arch; *K*, persistent left superior vena cava; *L*, esophagus; *M*, descending aorta; *N*, inferior vena cava.

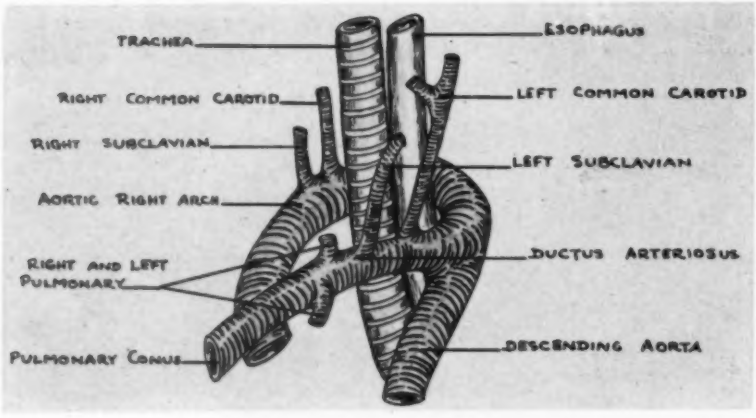

Fig. 3.—Left lateral view illustrating the congenital anomalies of the aortic system.

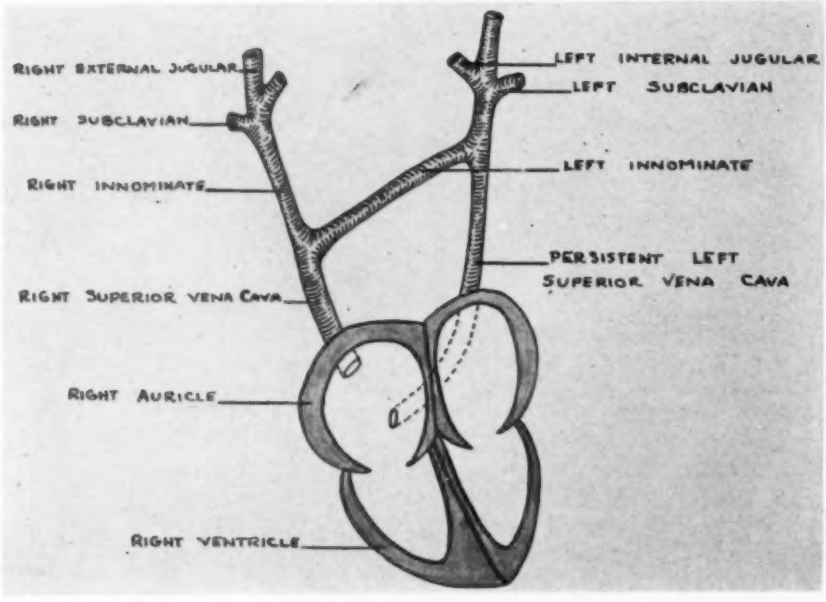

Fig. 4.—Ventral view illustrating the congenital anomaly of the venous system.

Since the first of the vascular anomalies described in this report (Case 1) concerns the venous system, a brief résumé of the formation of the superior vena cava follows: The paired anterior cardinal veins pass caudally from the jugular foramen to Cuvier's ducts on each side as the internal jugular veins. In the neck region an asymmetrical organization of the venous system is accomplished through the development of the left innominate vein. This vein arises from the left internal jugular vein and passes obliquely and to the right to fuse with the right internal jugular vein. The segment of the left internal jugular vein which remains between the innominate bifurcation and the left duct of Cuvier becomes obliterated; however, it persists as the ligament of Marshall. That portion of the right internal jugular vein caudal to the junction of the left innominate vein with the right duct of Cuvier becomes the definitive superior vena cava.

To explain the congenital vascular anomalies reported in this child, probably some developmental defect occurred during the fourth to seventh week of intrauterine life, or at about the time the vascular tree was in the process of development (Figs. 3 and 4). The defective growth caused changes as follows (1) The fourth aortic left arch (which normally becomes the definitive aorta) atrophied and the aortic right arch persisted as the definitive aorta. (2) The ductus arteriosus drew the aortic right arch sharply to the left (posterior to the esophagus and trachea), fused with it, and thus produced a vascular ring. Following the anastomosis of the aortic right arch with the ductus arteriosus, the aorta descended in the usual manner on the left side as the descending aorta. (3) Due to the absence of the aortic left arch, the left common carotid artery and the left subclavian artery grew caudally and laterally to form an anastomosis with the ductus arteriosus. (4) It is difficult to explain the congenital absence of the innominate artery; however, Taussig[6] states this is not an unusual finding in the presence of a persistent aortic right arch. (5) Because that portion of the left internal jugular vein caudal to the junction of the left innominate vein and craniad to the left duct of Cuvier remained patent, there existed a left superior vena cava, which like its analogue on the right, emptied into the right auricle of the heart.

COMMENT

The clinical symptoms of cyanosis, labored respiration, and copious secretions of mucus from the nasopharynx probably resulted from compression of the trachea and esophagus by the vascular ring (aortic right arch and the ductus arteriosus). Sweet and associates[7] reported a vascular ring (aortic right and left arch) in a 3½-month-old infant which caused coughing, wheezy respirations, and feeding problems. In the case herein discussed (Fig. 3) it is deemed problematic whether or not ligation of the ductus arteriosus distal to the bifurcation of the pulmonary arteries would have been justified had the diagnosis been made ante mortem. One should consider that with ligation of the ductus arteriosus distal to the bifurcation of the left common carotid and left subclavian artery, the blood supply to the left side of the face, neck, and arm would have been venous.

Again, the presence of one congenital anomaly suggests the possibility of others.

CASE 2.—*Clinical Brief.* This 9-month-old male infant was admitted to St. Luke's Hospital in the service of Dr. S. C. Henn in critical condition on March 7, 1948, and died eight and one-half hours later. His mother was a primipara Negress in good general health without significant past or family history, but with a loud systolic cardiac murmur. Her blood Kahn test was negative. She had an uneventful pregnancy with a low forceps delivery, at term, of the 7 pound, 2½ ounce male infant. Despite a lusty cry and good color, he was unable to nurse and was placed on formula feeding. Physical examination revealed complete muscular flaccidity, mongoloid eyes, possible congenital cataracts, hypermobility of wrists, hips, ankles, and feet, normal little fingers, and no heart murmurs.

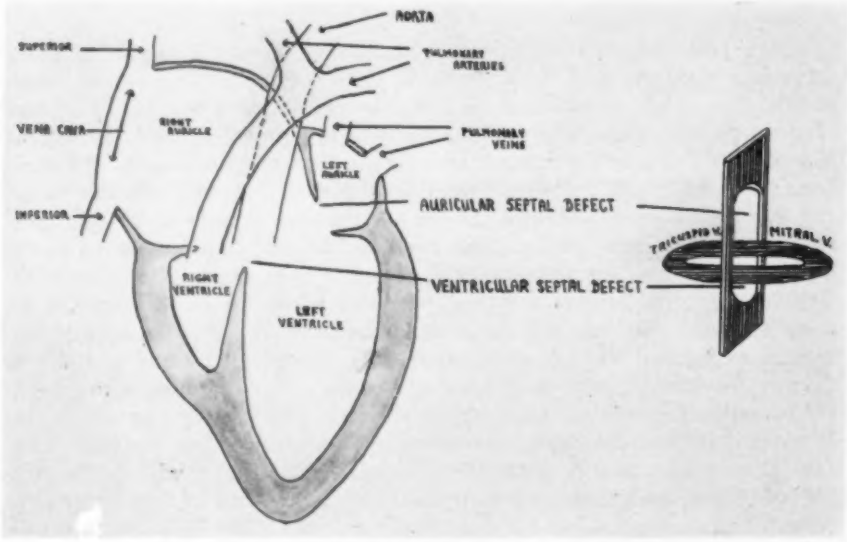

Fig. 5.—Diagram of the heart in Case 2 showing the persistent atrioventricular communis, underdeveloped right ventricle and left auricle, enlarged left ventricle and right auricle, and dextroposition of the aorta.

During the subsequent months he gained weight slowly, and at 5 months of age was circumcised. Three weeks before death he began to cough persistently and had a fever. A loud, systolic murmur then was heard over the entire precordium for the first time. On the day before admission to the hospital the mother noticed that the baby did not eat well and that his cough was worse. By the next morning when he was brought to the hospital, he had marked retraction of the soft muscles of the thorax with inspiration because of dyspnea. His rectal temperature was 105.8° F., his respiratory rate was 80, and his pulse was too rapid to be counted. The lungs had moist râles and a left pleural friction rub. The left lobe of the liver was palpable at the umbilicus. Subcutaneous fluids, penicillin, sulfadiazine, aspirin, and oxygen were started and the baby's rectal temperature dropped to 102° F. two hours later and the heart rate was reduced. With the latter a gallop rhythm was evident. However, his condition did not improve and he died a short time later. The clinical diagnosis was congenital heart disease with chronic heart failure, bronchopneumonia, and Mongolian idiocy.

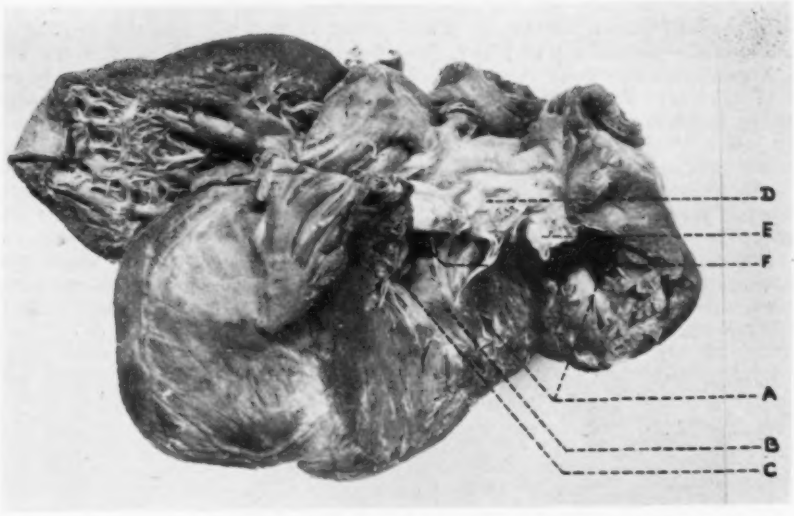

Fig. 6.—Posterior view of the heart in Case 2 illustrating *A*, the small size of the right ventricle; *B*, the interventricular septum; *C*, the interventricular septal defect; *D*, the right part of the anterior valve leaflet; *E*, the right lateral valve leaflet; and *F*, the space under the anterior leaflet.

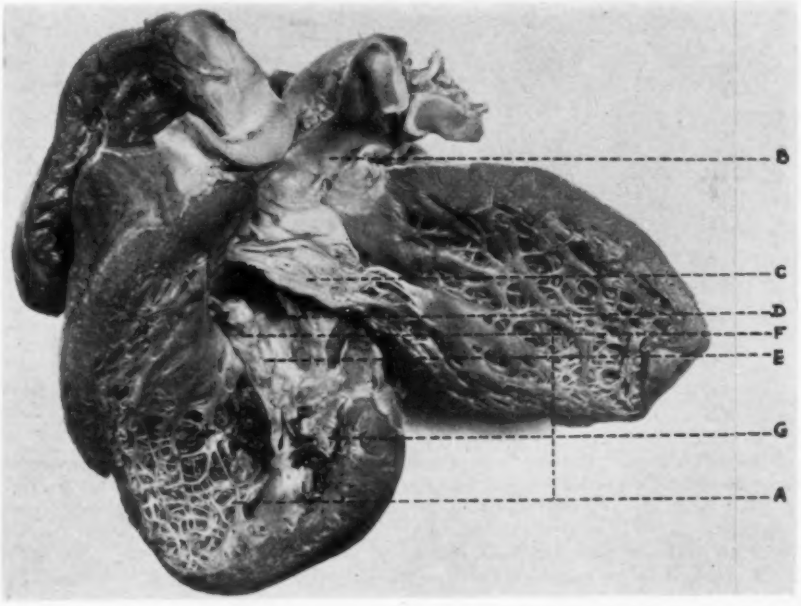

Fig. 7.—Left anterior view in Case 2 of *A*, the opened enlarged left ventricle; *B*, the dextroposed aorta; *C*, the left part of the anterior valve cusp; *D*, the interventricular septal defect; *E*, the posterior valve cusp; *F*, the space under the posterior valve cusp and *G*, the left lateral valve cusp.

Necropsy.—The body of this well-nourished Negro male infant weighed 5,450 Gm., was 65 cm. long (normal for this age, 8,000 Gm. and 67 cm.), had mongoloid features, and had an anterior fontanelle 2 by 2 cm. There were moderate ascites, bilateral hydrothorax, and hydropericardium. Focal regions of bronchopneumonia, hyperemia, and edema were present in the lungs. The liver had a chronic passive hyperemia. The greatly enlarged, abnormally shaped heart weighed 85 Gm. (normal for this age, 37 Gm.). Most of the enlargement was in the dilated right auricle and left ventricle because the left auricle and right ventricle were small by comparison. There were no venous anomalies. A probe introduced into the heart through the pulmonic artery passed only into the right ventricle, but when introduced through the aorta passed easily into either the left or right ventricle (see Fig. 5).

The left and right ventricular walls were each one centimeter thick. The length of the left ventricle from the attachment of the atrioventricular valve ring to the apex was 5.4 cm. in contrast to a corresponding measurement in the right ventricle of 2.5 cm. (Figs. 6 and 7). There were thin membranous eustachian and thebesian valves.

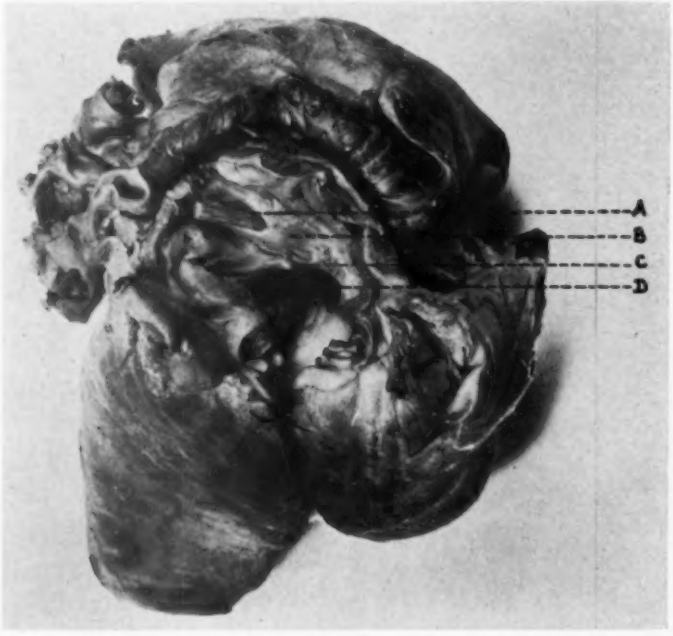

Fig. 8.—Photograph looking down into the left auricle in Case 2 illustrating *A*, the patent foramen ovale with a probe through it; *B*, the interauricular septum; *C*, the free edge of the interauricular septal defect and *D*, the left atrioventricular orifice.

The interauricular septum above was complete although the fossa ovalis was patent through an oblique channel 0.3 cm. in diameter (see Fig. 8). The septum deviated markedly to the left inferiorly and was incomplete through an opening 1.3 cm. anteroposteriorly and 0.5 cm. above the common atrioventricular ring. Its crescentric free border formed the right part of an oval left atrioventricular ostium 1.5 cm. in diameter (Fig. 8). The septum primum appeared to be well developed, but the septum secundum was not well formed, especially in the anterior portion.

The interventricular septum was complete in its lower part, but above it was incomplete. Its free margin was 1.2 cm. to the right of the lower free border of the interauricular

septum. The free border of this septal defect arched downward from the attachments of the common atrioventricular valve cusps 1 cm. and was 1.3 cm. in its anteroposterior measurement to form an opening through which the ventricles communicated freely (Fig. 7).

There was a single large atrioventricular orifice. Its right half functioned as the right atrioventricular orifice, but its left half or one-fourth with the interauricular septal defect functioned as the left atrioventricular orifice as previously described. The large orifice was guarded by a valve composed of four segments, one large anterior segment partially divided at the interventricular septum so that the right half corresponded to the anterior leaflet of the tricuspid valve (Fig. 6, *D*). At the right and left ends of the orifice were small leaflets somewhat corresponding to the posterior cusps of the usual valves (Figs. 6, *E*, and 7, *G*). Posteriorly over the free edge of the septal defect more on the right than on the left was another large, somewhat central leaflet probably representing the medial cusp of the tricuspid valve (Figs. 7, *E*, and 9, *E*). It was attached closely to the free margin of the underlying septum by a group of short chordae tendinae, thus leaving little communication between the ventricles in this location (Fig. 7, *F*). The defect under the anterior segment was deep with three chordae tendinae about one centimeter long (Fig. 6, *F*).

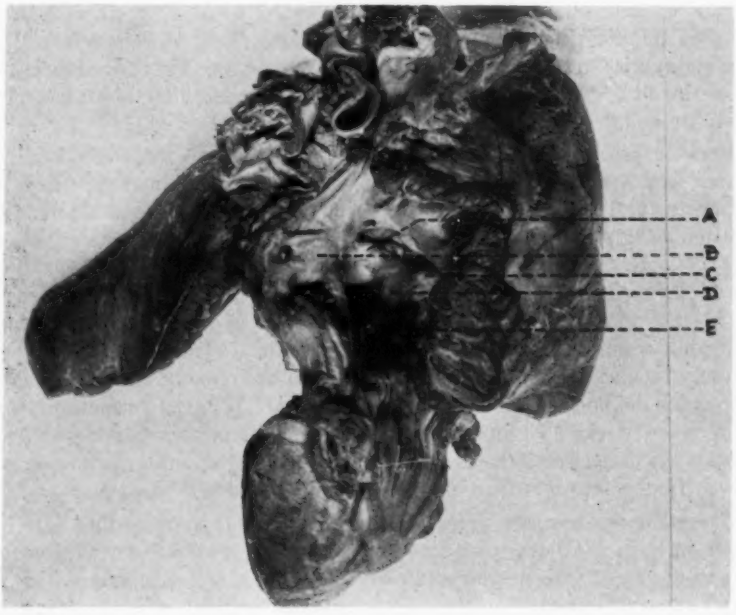

Fig. 9.—Photograph of the formalin fixed heart in Case 2 looking down into the right auricle illustrating *A*, the right part of the anterior valve leaflet; *B*, the interauricular septum; *C*, the right lateral valve leaflet; *D*, the displacement of the interventricular septum to the right; and *E*, the posterior valve leaflet.

The orifice of the aorta which was located to the right straddling the interventricular septal defect was in front of the anterior leaflet of the atrioventricular valve. Under slight tension the circumference of the aortic valve ring was 3.4 cm. and its leaflets were fenestrated near the commissures (Fig. 7). The orifice of the pulmonic artery was pushed to the right by the dextroposition of the aorta. Its leaflets also were fenestrated, and the circumference of the pulmonic ring was 3.1 cm.

The vessels leaving the heart were normal in size and without anomalies. The ductus arteriosus was closed. There were no other significant gross findings.

Histologically, sections of tissues stained with hematoxylin and eosin revealed marked chronic passive hyperemia of the lungs, liver, and spleen, and slight bronchopneumonia.

DISCUSSION

Congenital cardiac terata are reported to be caused by numerous factors, as hereditary influences, dysontogenesis, various infections of the mother such as syphilis and rubella early in pregnancy, poor prenatal diet, maternal hormonal and metabolic imbalances, and many others. In this case, as in most, there is no evident material or fetal etiology. About one-half of the reported cases of the cardiac malformation have occurred with Mongolian idiocy.[8] This would seem to indicate that the phase of fetal development during which this or a similar heart anomaly occurs is approximately at the same phase during which mongolism occurs. Consequently, an arrest of the forming fetus at this time results in both anomalous conditions.[6] Because numerous cases of normal offspring of Mongolian idiots have been reported, most authorities do not believe that the condition is due to hereditary factors.[3] By analogy, the same reasoning applies to the cardiac anomaly here discussed. Furthermore, in known cases of insult to the developing embryo from a rubella infection in the mother early in pregnancy, similar heart malformations have resulted.[10]

Because embryologists are not entirely agreed as to the method of fusion of these four heart structures—the endocardial cushions, interauricular, interventricular, and bulbar septums—an exact explanation of the mechanism of formation of septal defects associated with a common atrioventricular orifice is not possible. However, following the ideas advanced by Arey[5] on development of the normal human heart, the anterior and posterior endocardial cushions fuse in the midline in a figure-of-eight fashion dividing the common atrioventricular canal into a right and a left channel. Meanwhile, the septum primum, growing down from above, attaches to the already merged endocardial cushions by the end of the sixth week of embryo (12 mm.) formation. At the end of seven weeks (17 mm.) the septum membranaceum has closed by proliferation of tissue from the endocardial cushions, completing formation of the interventricular septum which has been growing up from below.

Therefore, in the case presented in this paper it appears that late in the fifth or early in the sixth week some growth defect occurred, preventing formation and fusion of the anterior and posterior endocardial cushions so that there was no place to which the descending septum primum and ascending interventricular septum could attach.

The small size of the right ventricle and dextroposition of the aorta can be explained on the basis of Spitzer's theory of incomplete rotation and torsion of the developing fetal heart.[11] Normally, during the fifth and sixth weeks of embryo formation the simple tubelike heart of preceding weeks grows faster than its pericardial sac, forming a spiralled S shape. The chief primary flexure is to the right, and by means of it the bulbus and ventricle become a U-shaped loop (the right limb or bulbus part forms the right ventricle and the left limb

forms the left ventricle). The origin of the aorta and pulmonary arteries is brought about through longitudinal ridges developing in the superior bulbus and fusing to create a septum. Apparently in the case under discussion the right limb of the loop failed to descend caudal enough or rotate to the left enough, resulting in underdevelopment of the right ventricle and dextroposition of the aorta.

The marked dilation of the right auricle is due to the displacement of the interauricular septum to the left, thereby decreasing the size of the left auricle and increasing the size of the right. Also, the ventricular pressure was transmitted to the right auricle through the markedly incompetent common atrioventricular valve, thereby leading to the dilatation of the thin auricular musculature.

Comment.—In this case, as in the first, some defect occurred during the fifth or sixth week of fetal growth, resulting in an incomplete torsion of the heart, failure of growth and fusion of the endocardial cushions, and Mongolian idiocy.

SUMMARY

Two cases of congenital heart disease are presented: one showed an aortic right arch and left descending aorta, a persistent left superior vena cava, and anomalous origin of the left common carotid and left subclavian arteries from the ductus arteriosus; the other showed an atrioventricular communis, dextroposition of the aorta, underdevelopment of the right ventricle and left auricle, and enlargement of the right auricle and left ventricle.

Such congenital vascular and cardiac anomalies are frequently associated with other anomalies. In the first case, the ear lobes were absent and the testicles were undescended. In the second case, the child was a Mongolian idiot.

In reviewing the literature, we were unable to find any similar descriptions of the anomalies reported above. Due to the important role which surgery now holds in the correction of many similar congenital vascular diseases, these two cases are presented.

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RADIATION THERAPY FOR WILMS' TUMOR OF THE KIDNEY

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WILMS' tumor may be treated surgically, radiologically, or by a combination of both therapies. A more detailed study of these methods shows that the management of the patients actually falls into five classes, each of which has its worthy exponents. The classes are as follows:

1. *Operation Alone:* The surgical treatment consists of nephrectomy through the lumbar route or transperitoneally. Ladd[1, 2] is the outstanding advocate for this method. All surgeons recognize, however, that this procedure is of no avail in the presence of pulmonary or other metastases. As frequently happens, the tumor mass may be too huge for removal, when first seen, although Ladd has been successful in removing tremendous growths by the transperitoneal approach.

2. *Operation and Postoperative Irradiation:* This combined method was probably the treatment of choice until recently. The postoperative irradiation destroys the embryonic malignant cells which have been inadvertently disseminated or left behind during surgical removal. Among others, Nesbit,[3] Hazzard,[4] Weisel,[5] and Priestley[6] advocated this method, although the latter now states that the combined method of pre- and postoperative irradiation may offer the best possibilities.

3. *Preoperative Irradiation and Operation:* For those who find the growth too massive for removal when first observed, a course of high voltage roentgen treatments is administered. The tumor is thus sufficiently reduced in size so as to permit surgical extirpation. An inoperable mass is rendered operable. Randall,[7] Kerr,[8] and others support this method of approach. The prenephrectomy irradiation not only shrinks the huge mass but also minimizes local and widespread dissemination of the embryonic tumor cells by sealing off the blood vessels and the lymphatics.

4. *Preoperative and Postoperative Irradiation:* This is the treatment of choice today, being advocated by a majority of the workers in this field. Among its advocates may be mentioned Adams,[9] Campbell,[10] Rowe,[11] Priestley,[12] Mertz,[13] Higgins,[14] Kretschmer[15] and others. The full advantages of both surgery and irradiation are embodied in this method.

5. *Irradiation Alone:* Radiation therapy alone is considered by some workers as the treatment of choice. They regard the growth as too dangerous to remove surgically because of its tendency to metastasize. Being highly malignant, Wilms' tumors are extremely radiosensitive and are considered, therefore, to be a radiation problem. Among the supporters of treatment by irradiation alone may be mentioned Dean,[16] Barringer[17] and others. It is well to mention here that inasmuch as the entire treatment is dependent upon irradiation without surgery, the cycle of roentgen treatments should be intensive. It is gen-

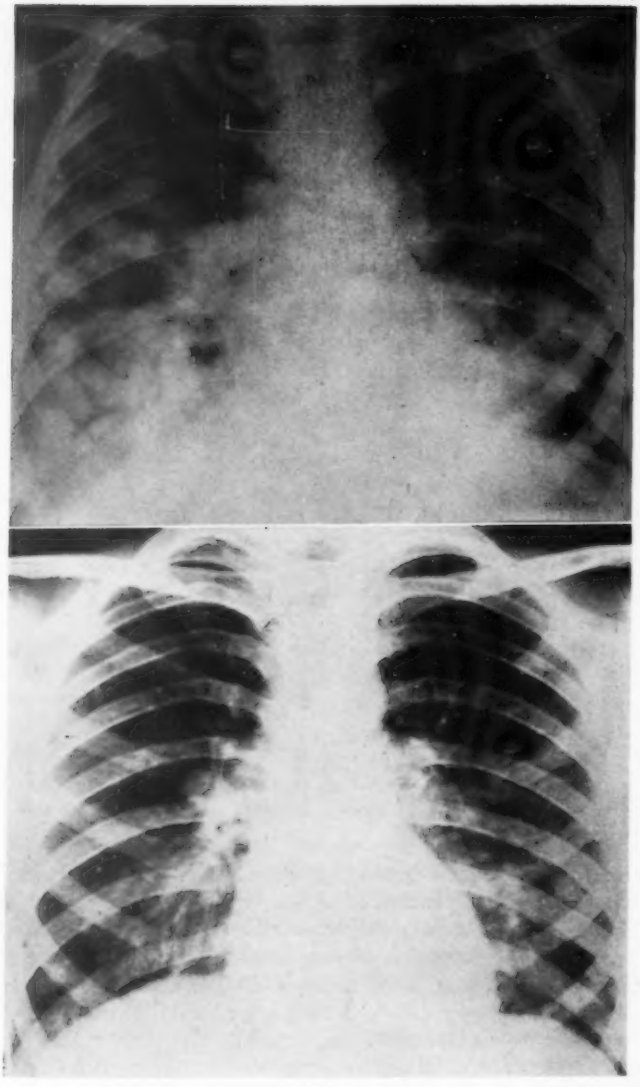
erally conceded that irradiation alone is the treatment of choice in the presence of metastasis, as nephrectomy is contraindicated (Fig. 1). Roentgen therapy under such circumstances is administered for palliation only. It is therefore wise to take roentgenograms of the chest and skeletal system to rule out the presence of metastases when surgery is contemplated (a radiologic procedure which should be routine for all patients when first seen).

Fig. 1.—H. S., a 9-year-old girl, whose symptoms were: a large mass in right abdomen; loss of weight; tiredness and cough with one episode of hemoptysis of two weeks' duration. Bilateral pyelography showed a tremendous right renal tumor. She received x-ray therapy alone with marked reduction in size of the mass. Operation was contraindicated because of extensive lung metastases (see Fig. 2).

Radiation Technique.—The technical factors involved in the roentgen treatment of Wilms' tumors depend on the age and general condition of the patient and the size of the tumor. One should also take into account whether the series of treatments is merely for palliation alone (as in cases with metastases) or whether nephrectomy is contemplated. Usually three portals of entry are employed over the mass, an anterior, a lateral, and a posterior field. Occasionally in a massive lesion six portals are preferable in place of three large areas. The advantages of multiple small portals are, first, a greater total dose can be given without permanent damage to the skin; second, more accurate cross-firing of the tumor may be thus obtained, and third, there is less likelihood of radiation sickness when small portals are used. The tissues surrounding the tumor mass should be included in the irradiated field.

The total dosage varies from 3,600 to 6,000 r. The treatments are given daily, one portal being treated when only three are mapped out over the mass.

A.



B.

Fig. 2.—Same patient as in Fig. 1. *A*, Extensive pulmonary metastases before roentgen therapy. *B*, Pronounced improvement two months after treatments. Child died six months after initial visit. Post-mortem examination revealed a Wilms' tumor of the right kidney with vascular invasion involving the pulmonary artery and the left ventricle and with metastases to the liver, lungs, retroperitoneum, and genital tract.

or two portals are given daily when six of smaller size are employed. No more than a total of 200 r in either case is given daily with the following technical factors: KVP 200; T.S.D. 50 cm.; portals 6 by 8 cm. or 10 by 10 cm.; H.V.L. 1.8 mm. of cu. The cycle of treatments is usually completed in from three to five weeks. In order that the full effects of the irradiation are obtained, operation, if it is to be performed, should be delayed for from four to six weeks after the completion of the course of roentgen treatments. After such a waiting period there is no detrimental effect to prevent prompt healing of the surgical wound.

In younger subjects (2 to 4 years of age), the total dosage should be slightly less than in a child of 8 or 9 years. A malnourished baby is usually less able to tolerate a full course than an older, well-nourished child.

The treatment of metastatic lesions is palliative and is similar to the roentgen treatment for the primary lesion. In the chest, irradiation is directed through three or more small portals for each lung and no more than 200 r is delivered daily for a total of 800 to 1,200 r for each field. The radiosensitivity of the tumor is evident by the rapid initial improvement, which, however, is short-lived (Fig. 2).

ANALYSIS OF CASES

From 1930 to 1947, seventeen patients with Wilms' tumor were treated. The youngest was 3 months of age, the oldest 10 years. There were ten male and seven female patients in the group. In all of the patients the duration of symptoms was less than six weeks. All of these children are dead, the longest survival being fourteen months. The average survival among the seventeen cases was six and one-half months.

Four patients received pre- and postoperative x-ray therapy, with an average survival of six and one-half months. Although this survival rate is the same as for the entire group of cases, it must be borne in mind that these four patients had the largest tumors which prompted their referral by the surgeon for preoperative irradiation.

Five patients were treated without surgical intervention because of demonstrable metastasis. The average survival of these patients who received roentgen therapy alone was only four and one-half months, even though both the tumor mass and the metastatic foci (lungs) were adequately irradiated. These patients presented a hopeless outlook at the initial examination.

Eight patients received only postoperative roentgen treatments with a survival of eight and one-half months. In evaluating this longer survival rate, one must take into account the fact that they represented the more favorable cases, being operable both from the standpoint of size of the neoplastic mass and of freedom of distant metastases.

CONCLUSIONS

From this inadequate series it is unwarranted to draw any accurate conclusions. It is evident, however, that the present management for this malady is deplorable. Although an occasional survival is reported in the literature, the mortality is near 100 per cent. With our present-day armamentaria little improvement can be expected. Yet every effort should be made to salvage as many

as possible from what seems to be an inevitable fate. Frequent periodic examinations of all infants including careful palpation of both kidneys should be a routine matter. In this way it may be possible to recognize these cases at an earlier stage. There is an imperative need for closer cooperation between the surgeon, radiologist and pediatrician or family doctor. From our present knowledge an adequate course of pre- and postoperative irradiation to the tumor bed offers the best possibilities.

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A NOTE ON METHEMOGLOBINEMIA AND HEINZ BODY FORMATION IN CATS FED COMMERCIAL CRAYONS

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CLINICAL reports have appeared recently concerning intoxication from ingestion of wax crayons.[1-3] Infants after eating red, orange, or yellow crayons developed cyanosis, methemoglobinemia, and other manifestations of poisoning by aromatic amines. There seemed to be a need for investigating this problem in experimental animals and consequently the studies reported here were undertaken in which crayons were administered to cats.

PROCEDURE

Test crayons bearing labels of commonly used brands were obtained on the open market. Healthy cats were used which weighed 2.5 to 5.5 kg. and had become well acclimatized to the laboratory environment. In the first group of tests, crayons dissolved in corn oil were fed by stomach tube. Later tests consisted of feeding crayons incorporated in fish, or the regular ground meat diet, to fasted animals. Methemoglobin (MHb) and total hemoglobin (Hb) were measured in blood samples obtained by venipuncture from the saphenous vein employing the method of Andrews and Horecker.[4] Heinz bodies were looked for in methyl violet-stained blood smears.[5]

RESULTS

Results of tube-feeding crayon in 25 to 50 c.c. of corn oil are shown in Table I. No increase in blood MHb level was observed. The normal range of MHb concentration in cat blood as judged from examination of one or more blood samples from sixty cats (other than those used in this work) can be said to be between 0.0 and 0.9 Gm. per cent MHb. Heinz bodies did not appear in the blood smear twenty-four or forty-eight hours after intubation, but a lipemia-like turbidity was noted in the sera for several hours. There was no objective evidence that the cats were injured in any way by the test.

TABLE I. EFFECT OF FEEDING CRAYONS IN CORN OIL BY STOMACH TUBE ON BLOOD MHb

CAT	GM. OF CRAYON ADMINISTERED	COLOR OF CRAYON	GM. MHb PER 100 ML. BLOOD ACCORDING TO TIME IN HOURS AFTER INTUBATION				
			0	3	4¾	6⅞	24
A	6.7	Red* and Blue	0.2	0.2	0.3	0.3	0.3
B	5.9	Yellow	0.2	0.2	0.1	0.0	0.0
C	4.1	Red* and Blue	0.1	0.4	0.2	0.0	0.4
D	4.8	Red* and Blue	0.4	0.4	0.3	0.0	0.9
E	4.5	Red* and Blue	0.6	0.3	0.0	0.0	0.4
F	4.1	Yellow	0.1	0.0	0.3	0.0	0.3

*In equal proportions.

From the Laboratory of Physical Biology, National Institutes of Health.

TABLE II. METHEMOGLOBINEMIA AFTER INGESTION OF CRAYON IN THE DIET

EXPERIMENT	CAT	GM. OF CRAYON EATEN	COLOR OF CRAYON	GM. MHb PER 100 ML. OF BLOOD ACCORDING TO TIME IN HOURS AFTER OFFERING CRAYON MEAT MIXTURE										PER CENT ERYTHROCYTES CONTAINING HEINZ BODIES 24 HR. AFTER EXPOSURE
				0	4	5	7	8	24	26	30	48	72	
1	1	11.9	Orange	0.7	0.5	0.1			0.7					
	2	14.3	Brown	0.4	0.1	0.3			0.0					
	3	14.5	Red	0.2	0.0	0.3			0.7					
	1-A	11.1	Red			1.8	2.7	1.7	2.1			0.6	0.5	
	2-A	10.4	Blue			0.0	0.4	0.7	0.0					
	3-A	14.3	Green			0.0	0.0		0.2					
2	1-B	10.7	Red	0.0	0.0	0.1			0.1					
	2-B	16.1	Yellow	0.0	0.7	0.7			0.4					
	3-B	16.1	Purple	0.2	0.2	0.0			0.4					
	1-A	10.7	Red	0.9	0.4				0.7					
	4	16.1	Orange	0.2	0.6	0.1			0.6					
	5	8.6	Orange	0.2	0.2	0.1			0.3					
	6	8.6	Red-Orange	0.1	0.0	0.4			1.6	1.5	2.1	1.2	0.3	
	7	8.6	Yellow	0.4					0.6	0.1		0.1		
	8	8.6	Green	0.4					0.3	0.7		0.0		
	9	8.6	Red	0.4					0.2	0.0		0.7		
	10	8.6	Red and Red-Orange	0.3					0.2	0.4		0.4		
	11	8.6	Orange and Red-Orange	0.2					0.2	0.0		0.2		
3	1-C	8.0	Orange	0.1			0.0		0.0					4
	1-A	8.0	Red	0.2			0.3		0.3					11
	2-C	2.9	Yellow	0.1			0.7							6
	3-C	8.0	Red	0.2			1.6		1.8			0.4		98
	4-B	15.0	Yellow	0.1			0.4		0.0					3

Findings obtained in three experiments in which crayon was offered in the diet to fasted cats are presented in Table II. In three of the twenty-three exposures a moderate and prolonged methemoglobinemia developed with about 20 per cent of the pigment oxidized at the peak of the curve. The duration of the methemoglobinemia is comparable to that reported in human beings. Numerous large Heinz bodies were observed in the twenty-four- and forty-eight-hour blood smears of the positive cats in the first and second tests. Heinz body counts in the third experiment revealed a high percentage of these bodies only in the cat with methemoglobinemia. Because the proferred crayon-meat mixture was eaten after a variable and sometimes undetermined delay, the time intervals in the table do not relate to time when exposure to crayon began.

It is noteworthy that none of these animals presented any objective external manifestation of intoxication other than perhaps a slight apathy during methemoglobinemia.

DISCUSSION

From the data presented it is apparent that methemoglobinemia and Heinz body formation occur in a small percentage of cats fed commercial crayons. The results are more striking if only animals fed red or red-orange crayons are considered, in which group, one-third of the exposures resulted in MHb and Heinz body formation. No conclusion can be drawn from these results regarding poisoning in human beings. Relatively very large doses were given without evidence of serious intoxication other than the methemoglobinemia which per se is innocuous. Cats, it should be recalled, are probably the most susceptible species to methemoglobinemia. Possibly, however, the response of cats to oral crayon might prove useful in establishing, with further studies, the mechanism whereby crayons are toxic after ingestion by infants. A means is available perhaps to test the two postulates—individual idiosyncrasy vs. toxic contamination of the red dye. The latter point of view agrees better with the finding that the reaction was inconstant in one of our animals.

SUMMARY

Methemoglobin and Heinz body formation were observed in a small percentage of cats fed wax crayon in their diet.

The authors are indebted to Mr. E. C. Thompson for the Heinz body determinations.

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A NOTE ON POISONING DUE TO INGESTION OF WAX CRAYONS

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SINCE the first published report on "Poisoning Due to Ingestion of Wax Crayons,"[1] several other cases have been described.[2-4] In addition to these, Dr. H. Russell Irwin,[5] Children's Hospital, Los Angeles, has observed four more cases. We have also been informed that, during the past two or three years, seven cases of poisoning by wax crayons have been brought to the attention of one of the leading distributors of school supplies. Details of these latter observations are not known to us. The picture of the other cases seems to be rather uniformly that of acute, severe methemoglobinemia.

So far, four different brands of wax crayons of red-orange, orange, yellow, and violet color have been found involved. According to the manufacturers, parared is used in the red-orange and orange, and benzidine yellow in the yellow crayons. As reported before,[1] our own examination has shown the presence of parared in orange and red-orange crayons (two brands), while the red and yellow-orange crayons were free of it.

Parared was originally produced by coupling diazotized paranitraniline with β-naphthol. This compound has been found to be slightly soluble in water. Hence, the parared used in dyeing cotton is now made by coupling paranitraniline with Naphthol-AS and similar amides.[6] The pigment used in wax crayons is chlorinated parared, as stated by the manufacturers. A sample of this pigment was examined, and also a sample of parared.* Both pigments were, as far as we could ascertain, practically insoluble in water or in standard solvents with the exception of benzol. Parared was added to stomach fluid of pH 1.1 to 8.15, shaken in a Waring Blendor, incubated for twenty-four hours at body temperature, and shaken again. After filtering, the fluid did not contain parared. The same results were obtained with chlorinated parared.

In contrast to the results recorded in the preceding Note[7] and obtained by Irwin,[5] we have not been able to produce methemoglobinemia in dogs or rabbits after feeding or injecting intravenously large doses of the pigments. However, in comparing these results with Dr. Spicer's and Dr. Irwin's findings, it has to be kept in mind that cats respond much more readily to methemoglobin-forming substances than dogs or rabbits.

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From the Department of Preventive Medicine, The Jefferson Medical College of Philadelphia.

*Provided by E. I. DuPont de Nemours and Company, Inc.

THE TOXICITY OF WAX CRAYONS IN ANIMALS

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TOXIC manifestations in children following the ingestion of wax crayons have been reported recently.[1, 2, 3] These symptoms were similar to those observed in acute aniline poisoning. The children were cyanotic and dyspneic, suggesting a considerable degree of methemoglobinemia. In one of the reported cases the presence of considerable methemoglobin was confirmed by chemical analysis.[3] This subject, who also showed Heinz bodies, exhibited a rapid lessening of cyanosis following the administration of methylene blue. In another of the cases a moderate urinary elevation of bilirubin and urobilinogen was reported.[1] It should be noted that in none of these cases was methemoglobin formed when cats were fed the crayons which caused the illness in the children.

The problem under discussion is one of acute and not chronic poisoning. Studies on the toxicity of the crayons and the pigment used in them are reported below. Methemoglobin formation, leucopenia, and, in some cases, Heinz body formation was measured as an index of the toxicity of the material studied.

MATERIALS AND METHODS

Orange and yellow crayons have been chiefly involved in the reported cases. Studies were therefore confined mainly to these crayons. Various pigments commonly used in crayons were also tested. These pigments were lakes of the dyes parared, chlorinated parared, and benzidine yellow.

Methemoglobin was determined by a slight modification of the method of Evelyn and Malloy.[4]

EXPERIMENTAL DATA

The Toxic Effect of Crayons and Pigments on Rats.—Young rats weighing about 125 Gm. were divided into three groups and treated as follows:

Group I: Chlorinated parared and benzidine yellow pigments were each fed to a group of six rats for six days in doses of 70 mg. to each rat. The pigments were suspended with gum arabic in the drinking water of the animals.

Group II: Twelve rats were deprived of food for thirty-six hours and then placed in individual cages, each containing a single crayon. Six rats were given the orange and six the yellow crayon. The crayons were consumed in all cases within twenty-four hours.

Group III: Six rats were set aside as controls.

At the end of twenty-four hours blood samples were withdrawn from the heart of rats of all three groups and examined for both methemoglobin and Heinz bodies. No significant difference between the rats of Group I and II was observed over those of the controls.

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The Effect of Crayons on Dogs.—Two dogs were fed one crayon daily for six weeks. During the first three weeks the dogs received yellow crayons; for the last three weeks orange crayons were given. Each week a different name brand was administered. Some crayons were suspended in oil, others which did not suspend well were incorporated in chopped meat.

TABLE I. METHEMOGLOBIN IN BLOOD AFTER THE ORAL ADMINISTRATION OF CRAYONS TO DOGS*

CRAYONS	METHEMOGLOBIN (PER CENT OF TOTAL HEMOGLOBIN)	
	DOG 1	DOG 2
Control	2.1	1.3
Yellow crayon 1	1.9	1.3
Yellow crayon 2	1.5	0.9
Yellow crayon 3	2.9	1.9
Orange crayon 1	1.8	1.3
Orange crayon 2	2.4	1.0
Orange crayon 3	1.6	0.9

*The dogs were fed a single crayon daily. At the end of each week a different brand or color of crayon was substituted. Methemoglobin determinations were made weekly.

Blood methemoglobins which were measured weekly showed no significant rise over the control levels (Table I). Hemoglobin, red cell count, and white cell count (total and differential) also showed no significant change. Para-aminophenol has been reported in the urine of the children who ingested crayons.[1] Examination of the urine of the dogs by methods previously described[5] revealed neither para-aminophenol (free and conjugated) nor aromatic amines.

The Effect of Pigments Administered Intravenously to Dogs.—Two dogs were given intravenously 75 mg. of pigment suspended in propylene glycol. One dog received parared pigment and the other chlorinated parared. Examination of blood periodically over a twenty-four-hour period showed no methemoglobin formation and no change in the white cells or hemoglobin. The lack of toxicity after parenteral administration suggests that the toxicity of the wax crayons does not depend upon absorption of this pigment from the gastrointestinal tract.

The Effect of Crayons on Cats.—Since cats are particularly susceptible to methemoglobin-forming agents, the effect of crayons was also studied on these animals.

TABLE II. METHEMOGLOBIN IN BLOOD AFTER THE ORAL ADMINISTRATION OF CRAYONS TO CATS*

EXPT. NO.	METHEMOGLOBIN (PER CENT OF TOTAL HEMOGLOBIN)		
	CONTROL	AFTER YELLOW-ORANGE CRAYON	AFTER YELLOW CRAYON
1	2.6	2.5	1.0
2	2.0	5.6	1.1
3	1.7	2.4	1.5
4	2.1	3.5	1.0

*The cats received one-half of a yellow-orange crayon mixed in salmon daily for four weeks, then similarly one-half of a yellow crayon daily for three days. Methemoglobin determinations were made at end of the period of each crayon feeding.

Four cats were given one-half of a yellow-orange crayon incorporated in fish daily for four weeks. Blood was then withdrawn under Nembutal anesthesia, and the methemoglobin determined. No significant changes were observed, either in the methemoglobin (Table II), in the hemoglobin, or in the white cells, as compared with control blood samples drawn prior to the experimental period.

The above cats were then given, in a similar manner, one-half of a yellow crayon adily for three days. Again no significant change in the blood picture was observed (Table II).

DISCUSSION

The toxic symptoms found in children can be ascribed to the formation of methemoglobin. This suggests the possibility that the azo dyes used in the crayon pigments change in the body to the toxic, aromatic amines. However, the feeding of wax crayons or pigments to animals failed to produce experimental methemoglobinemia. Although children commonly ingest wax crayons, the occurrence of toxic symptoms is rather rare. This suggests that the occasional toxicity of the crayons may be classed as an idiosyncrasy.

SUMMARY

The feeding of orange, yellow, and yellow-orange crayons to rats, dogs, and cats failed to produce methemoglobinemia. Administration of crayon pigments orally to rats and intravenously to dogs similarly failed to produce methemoglobinemia.

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NONSENSITIZATION TO REPEATED TUBERCULIN TESTING

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ALTHOUGH, it has been shown that tuberculin testing may cause local or systemic flare-ups[1-3] in patients with proved tuberculosis, the question often arises as to whether the various tuberculin tests can induce hypersensitivity to themselves in nontuberculous individuals.

Some investigators[4-7] have felt that it was possible to induce tuberculin hypersensitivity to tuberculin while others[8, 9] demonstrated that it was unlikely.

Since this is an important factor in patients being observed for the possible presence of tuberculosis, another study in an attempt to clarify this point would not be amiss. Furthermore, since the tuberculin patch test had not been used in any of the previous studies, this would be an opportune time to determine its status with regard to sensitivity.

Therefore, two groups of infants who were being kept as boarders on the wards and who had not been exposed to tuberculosis were included.

The Mantoux (intradermal) test using O.T. (prepared by the Bureau of Laboratories of New York City Department of Health) was used on a group of ten infants whose ages ranged from 2 to 9 months, and on one child 3 years of age.

In each case a 1:10,000 dilution was first given, and when found to be negative was followed by a 1:1,000, and then a 1:100 dilution. When the child's test proved negative to the latter, it was repeated at forty-eight hour intervals. The length of time between the first and last test varied from one to six months and the number of tests done from eleven to sixty, as noted in Table I.

TABLE I. MANTOUX TESTING

Case	1	2	3	4	5	6	7	8	9	10	11
Sex	F	M	F	F	M	M	F	F	M	F	M
Color	W	W	W	W	W	W	W	C	C	C	C
Age at onset (in months)	5	5	2	3	6	7	7½	36	9	1	2
Number of tests done											
December	3	3	3	3	3	3	3	3	3		1
January	8	8	8	8	8	8	8	7	8	1	1
February	3		3	3	3		1		3	2	2
March	15		15	15	7			15	12		15
April	12		12	12(3*)				12			12
May	15		15	2				5			15(1*)
June	4		4								4
Total number	60	11	60	43(3*)	21	11	12	42	26	3	49(1*)
Time between first and last test (in months)	6	1	6	5¼	2½	1	1½	4½	3	½	6

*Indicates the number of questionable reactions which are included in the total figure.

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In Case 4, there were three occasions on which an area of erythema was noted which disappeared after forty-eight hours and then was subsequently followed by negative results.

In Case 11, this occurred once and was similarly followed by negative results, giving the impression that it was a mild, local, inflammatory reaction.

Tuberculin patch test (Vollmer) was used on another group of eleven infants ranging in age from 2 to 10 months and on one child of 3 years.

It was applied over the interscapular area, read forty-eight hours after removal, and when negative was immediately followed by another one applied to another area.

This procedure was followed except for several patients of both groups, who were isolated in a contagious disease hospital during periods of contagion, at which time tests were not done.

From eight to twenty-nine patch tests were done on the infants over a period ranging from one to six months, as illustrated in Table II.

TABLE II. TUBERCULIN PATCH TESTING

Case	1	2	3	4	5	6	7	8	9	10	11	12
Sex	M	M	M	M	M	M	F	F	M	F	M	F
Color	W	C	W	W	C	W	C	W	C	C	C	W
Age at onset (in months)	2	7	4	4	5	10	7	3	8	36	2	4
Number of tests done												
December		2	2	2	2	2	2	2	2	2	2	2
January	1	7	7	7	7	7	7	7	6	6	7(1*)	6
February	3	3	3	2	3	2	1	2			3(1*)	
March	7		5		2	6	6(1*)	3		7(2*)	1(1*)	
April	7		7		3	3	3	7		5(1*)	4(1*)	
May	7		3			7	3	4		7	7	
June	2					2				2	2	
Total number	27	12	27	11	17	29	22(1*)	25	8	29(3*)	26(4*)	8
Time between first and last test (in months)	5	1½	4½	1½	4	6	4½	4½	1	6	6	1

*Indicates the number of questionable reactions which are included in the total figure.

In Case 7, there was one questionable reaction (area of erythema which disappeared within forty-eight hours) on March 29 but all subsequent tests were negative.

In Case 10, questionable reactions occurred on March 25 and 29 and on April 11, but all others that followed were negative.

In Case 11, similar questionable reactions occurred on January 27, February 2, March 5, and April 15, but all other tests were negative. Because of these questionable reactions, Case 11 (same as Case 11 in Table I) was also tested with O. T. forty-nine times and except for May 1, when a slight, transient erythema was noted, all tests were negative.

SUMMARY AND CONCLUSION

1. Twenty-three nontuberculous infants were tested for hypersensitivity to repeated tests of tuberculin using the patch test and the O.T.

2. No evidence of any definite or lasting sensitivity could be detected.

3. Therefore, it is felt that it should be safe to follow any suspicious cases with routine skin testing as long as no evidence of tuberculosis is proved.

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FAILURE OF GAMMA GLOBULIN TO PREVENT VARICELLA

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MOST physicians regard chicken pox as a rather benign disease which, except for the infrequent complication, is without serious consequence. However, in the institution, the pediatrics ward, the isolation hospital, or orphanage, it may assume an importance greater than that of a mere inconvenient nuisance. Cross-infections and sporadic outbreaks, once begun, may become recurrent every few weeks. This results in the tying up of wards for considerable periods of time. It may even cause the closing of an entire service. In any event, it seriously handicaps the normal operation of the unit.

For this reason, as well as for the protection of the occasional child at a period when varicella infection may not be desirable, an effective prophylactic measure would be of considerable value. The preparation of a vaccine is not likely, at least not until varicella virus has been transmitted to lower animals or their embryos, which transmission has not as yet been accomplished. From time to time claims have been made concerning the efficiency of pooled human adult serum or convalescent serum.[1] On the other hand, equally poor results have been reported,[2] and since these have been based on more thoroughly executed and carefully controlled experiments, they have been more convincing.

The excellent passive immunity afforded by human serum gamma globulin against measles[3] and infectious hepatitis,[4] its high scarlatina and diphtheria antitoxic titers, and its availability in generous amounts through the agency of the American Red Cross, prompted us to determine whether gamma globulin may not also contain an antivaricella factor and thus be of value in the prevention or modification of chicken pox. In two previous attempts, no significant results were obtained by Greenberg[5] with gamma globulin against rubella and varicella, while excellent results are claimed by Funkhouser.[6]

An opportunity to conduct our first trial appeared in April, 1946, when, in an orphanage housing forty-one children of both sexes, aged 3 to 5 years, five cases of varicella occurred, the first on April 7, a second on April 9, and three on April 10. The source of exposure was unknown.

On April 11, four days after exposure, the remaining children were divided into two groups. Group A consisted of thirteen children with histories of previous varicella infection. Group B was comprised of twenty-three children without histories of chicken pox, and this group was further subdivided into Group I, having ten children to be treated with gamma globulin, and Group II, with thirteen children to serve as untreated controls. After the treated group received 5 c.c. of gamma globulin intramuscularly, all of the children were permitted free and intimate contact with those having varicella.

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Four secondary cases appeared in the control group, one each on April 27, 29, 30, and May 11. A fifth case occurred on May 27, and a sixth on June 8. It was subsequently learned that three of the ten children inoculated had had chicken pox previously, leaving 7 in this group, none of whom contracted chicken pox.

Despite these promising results, it was felt that no conclusions were warranted at this point until they were amply confirmed by further trials. Later, two other occasions presented themselves and attempts to verify the original findings were made. These resulted in complete failure.

The second trial was conducted in a day nursery in May, 1947. There were approximately seventy-five children of both sexes, mostly of preschool and some of school age in attendance. A 6-year-old girl who had been previously well had complained of a stomach-ache on April 29. She had no fever at this time. On April 30, she appeared normal and had no complaints. That evening she broke out with "a few spots" on her body. She was brought into the nursery on May 1. On examination, she was found to have a generalized eruption and was sent home immediately, having had no contact with any of the other children at the nursery at that time. A physician who saw her at home the next day made a diagnosis of chicken pox. On May 6, the fifth day after exposure, upon being informed of the situation, twenty-three of the children at the nursery who had histories of not having had varicella previously were divided in half. Eleven of these received 5 c.c. of gamma globulin intramuscularly and twelve were untreated. Between May 14 and 27, six cases of varicella appeared in the treated group and six cases were observed between May 10 and 20 in the control group.

The third trial was carried out in the orphanage mentioned above in March, 1948. By this time, there had been a considerable turnover of inmates so that the majority of them had been newly admitted since the outbreak in 1946. On the sixth day of that month a child came down with chicken pox. On March 8, the second day after exposure, when our attention was called to this, there were forty children, fourteen of whom were said to have had chicken pox; the remaining twenty-six were divided into two groups of thirteen each. In the first group, each child received 10 c.c. of gamma globulin intramuscularly. The second group served as control. Between the nineteenth and twenty-third day of March, chicken pox occurred in seven of the inoculated and in eight of the uninoculated group.

It is interesting to note that four of the fourteen who supposedly had had chicken pox previously became infected on March 20. This demonstrates that because of the unreliability of histories in institutions, it is important to utilize large numbers of adequately controlled groups to ensure the validity of results.

Recently, at about the time of completion of our third series, a report by Funkhouser[6] appeared, describing four separate episodes where the treatment of groups of seven, sixteen, twenty-three, and thirty-one exposed children with 2 to 5 c.c. of gamma globulin gave 85 to 100 per cent protection against varicella. He was fortunate in being able to inject these children on the first day following appearance of the varicella lesions on the primary case. Perhaps this early

treatment may account for the disparity in our results, since our contacts were not inoculated until two to five days after the eruption appeared on the first case. Unfortunately, Funkhouser failed to include uninoculated controls. Because varicella is admittedly one of the most contagious diseases, with a high morbidity among susceptible contacts, Funkhouser's results appear highly suggestive. Nevertheless, the lack of controls detracts from the significance of his findings, for accurate interpretation and the evaluation of the validity of such results is rendered difficult, if not impossible, by the omission of suitable controls.

While we do not consider our results final, it would appear at this time that gamma globulin, given to children in 5 c.c. or 10 c.c. doses intramuscularly, is not an effective prophylactic measure against varicella, since it failed to prevent or modify the disease in two out of three controlled experiments where it was given two to five days after exposure. We do not know how to explain the contradictory results in our first trial where there was apparent protection by gamma globulin. Because histories in orphanages are frequently unreliable, it is conceivable that many more of the children than the three later discovered in the treated group may have had varicella previously.

It is possible that earlier administration may be of benefit, but even if true, it would not always be feasible and would be of limited practical value. This point, however, deserves further elucidation and opportunities will be sought to investigate the effect of gamma globulin administered on the first day following exposure to the erupted case and possibly also prior to exposure.

SUMMARY

In three series of experiments, children exposed to varicella were given 5 c.c. or 10 c.c. of gamma globulin intramuscularly, two to five days after the primary case with the erupted lesion appeared.

In the first series, five secondary cases appeared in thirteen untreated controls, while seven children inoculated with 5 c.c. of gamma globulin four days after exposure remained free of infection.

In the second series, six of eleven children treated five days after exposure and six of twelve controls developed chicken pox.

In the third series, seven of thirteen children treated two days after exposure and eight of thirteen controls developed chicken pox.

No explanation is evident for the apparent success in the first series, but it is possible that the histories of not having had varicella previously may have been unreliable.

Gamma globulin does not appear to afford passive immunity under the conditions of these experiments.

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ELECTROENCEPHALOGRAPHY IN BEHAVIOR PROBLEM CHILDREN

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SINCE 1937, when Solomon, Jasper, and Bradley[1] reported a high incidence of electroencephalographic abnormality in children with behavior disorders, there have been repeated reports in the literature confirming this original finding.[2-10] All reports but one indicate a 50 to 70 per cent incidence of electroencephalographic abnormality in behavior problem children. Jenkins and Pacella,[7] by contrast, report 22 per cent EEG abnormality in a group of fifty delinquent boys. The type of abnormality has been described as paroxysmal[2, 8, 9] or slow,[2-4, 6, 8, 9] with rare reports of focal abnormalities.[2, 3] The explanation of the high incidence of electroencephalographic abnormality has varied widely. Some authors suggest that certain children with behavior disorders possess the personality and electroencephalographic abnormalities of epileptics without clinical seizures.[2, 3] It has been suggested that the electroencephalographic abnormality indicates immaturity,[6] lack of control,[11] and disturbance of cortical function,[4] and that these traits characterize the personality disturbance as well as the electroencephalogram. Others suggest that the EEG and personality abnormalities are inherited traits in many instances.[9, 10] Finally, the opinion that EEG abnormalities in behavior problem children may be due to organic brain pathology is based on the following facts: organic pathology is known to be capable of producing EEG abnormality; some investigators have reported a correlation between EEG abnormality and a history suggestive of brain damage;[2, 5, 9] and an association has been reported between certain personality features, thought to be due to organic impairment, and EEG abnormality.[7] There is no direct evidence on the basis of other findings that organic impairment does, in fact, exist in some of these cases.

Greenblatt, Levin, and Atwell[12] have reported a series of adult patients suspected of having brain damage who were studied by means of psychological tests and EEG. They report greater accuracy for the psychological tests than for the electroencephalogram, but the greatest diagnostic accuracy was achieved by the use of both tests. Of the patients in whom both tests were abnormal, 91 per cent were diagnosed as having brain damage. Forty-three per cent of the patients in whom both tests were normal were diagnosed as having brain damage. The authors point out, however, that many of the patients had brain disorders which were either arrested or slowly progressive, and that a normal EEG may be found in spite of the presence of demonstrable organic pathology under these conditions.

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Sarason and Sarason,[13] working with familial defectives, were able to demonstrate a correlation between "organic" findings on psychological testing and EEG abnormality. The authors report a 60 per cent incidence of EEG abnormality in patients whose psychological test results suggested organic impairment, as against 18 per cent abnormality in patients who had no "organic" signs on psychological testing. The same authors[14] found the same correlation between EEG abnormality and organic signs on psychological testing in a group of cerebral palsied children, all of whom had neurological evidence of brain pathology. The authors conclude that both the psychological examination and the EEG are likely to demonstrate superficial organic brain pathology.

It was considered likely that the psychological test might provide valuable evidence as to the presence or absence of brain pathology in behavior problem children with abnormal electroencephalograms.

MATERIAL AND METHODS

The 160 subjects utilized in this study were all patients who had been referred for diagnostic electroencephalography by Dr. William B. Curtis.* Through his kindness, the clinical histories of these cases were made available and were reviewed for the following items: (1) family history of psychosis, alcoholism, epilepsy, or psychopathic personality; (2) medical history of chorea, encephalitis, meningitis, head injury with unconsciousness, severe illness with delirium or high fever occurring before the age of 2 years, or a history of abnormal birth (For the purposes of this study, an abnormal birth was indicated by a history of prematurity, multiple birth, instrument or breech delivery, cesarean section, or a history of neonatal anoxia. A history of one or more convulsions excluded the patient from the series); (3) abnormal neurological signs.

All the patients in this group had had psychological examinations as part of their diagnostic work-up. The original tests were reviewed by Dr. Seymour Sarason. Unfortunately, most of the children had been given the Stanford-Binet test, Form M. Because of the lack of performance items on this test, Dr. Sarason was able to separate only those in whom the evidence for organic factors was so strong that it could be clearly seen, even in the predominately verbal material.

Electroencephalograms were obtained with a six-channel Grass Electroencephalograph. Electrodes were placed on frontal, central, parieto-occipital, and temporal areas on both sides. Grounded, interconnected ear leads were used. All the electroencephalograms were reviewed and classified according to the Gibbs' classification,[15] as moderately slow (S_1), moderately fast (F_1), very slow (S_2), very fast (F_2), paroxysmal (petit mal, petit mal variant, psychomotor, spikes, or grand mal), or focal. Records in which slowing was confined to the occipital leads were classified separately. The normal control series consisted of 373 unscreened normal children, aged 2 weeks through 15 years. Of these records, 120 were obtained at the Boston Children's Hospital and were

*Dr. Curtis is in charge of Psychiatric Service in the Community, a Community Chest agency to which children in need of psychiatric opinion or aid may be referred by schools, courts, parents, other agencies.

made available through the kindness of Dr. Frederick A. Gibbs, and Mrs. Erna L. Gibbs. Two hundred fifty-three records were obtained at the Pediatrics Clinic of the New Haven Hospital, with the collaboration of Dr. Donal L. Dunphy.

TABLE I

SEX	NO. PATIENTS	ELECTROENCEPHALOGRAM			
		NORMAL		ABNORMAL	
		NO.	%	NO.	%
Male	123	85	69	38	31
Female	37	19	51	18	49

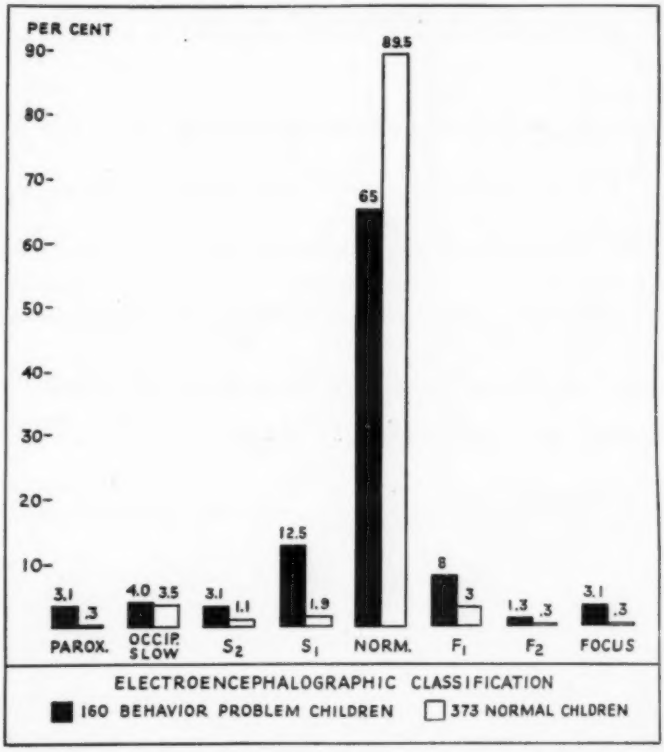

Fig. 1.—*Parox*, paroxysmal (petit mal spikes, paroxysmal slow); *Occip. slow*, occipital slowing; S_2, very slow; S_1, moderately slow; F_1, moderately fast; F_2, very fast.

RESULTS

Incidence of EEG Abnormality.—Of the 160 patients in this series, 56, or 35 per cent, have abnormal EEG's. The distribution of EEG abnormality in normal children is given for comparison. Examples of abnormal electroencephalograms from the behavior problem group are illustrated in Fig. 2.

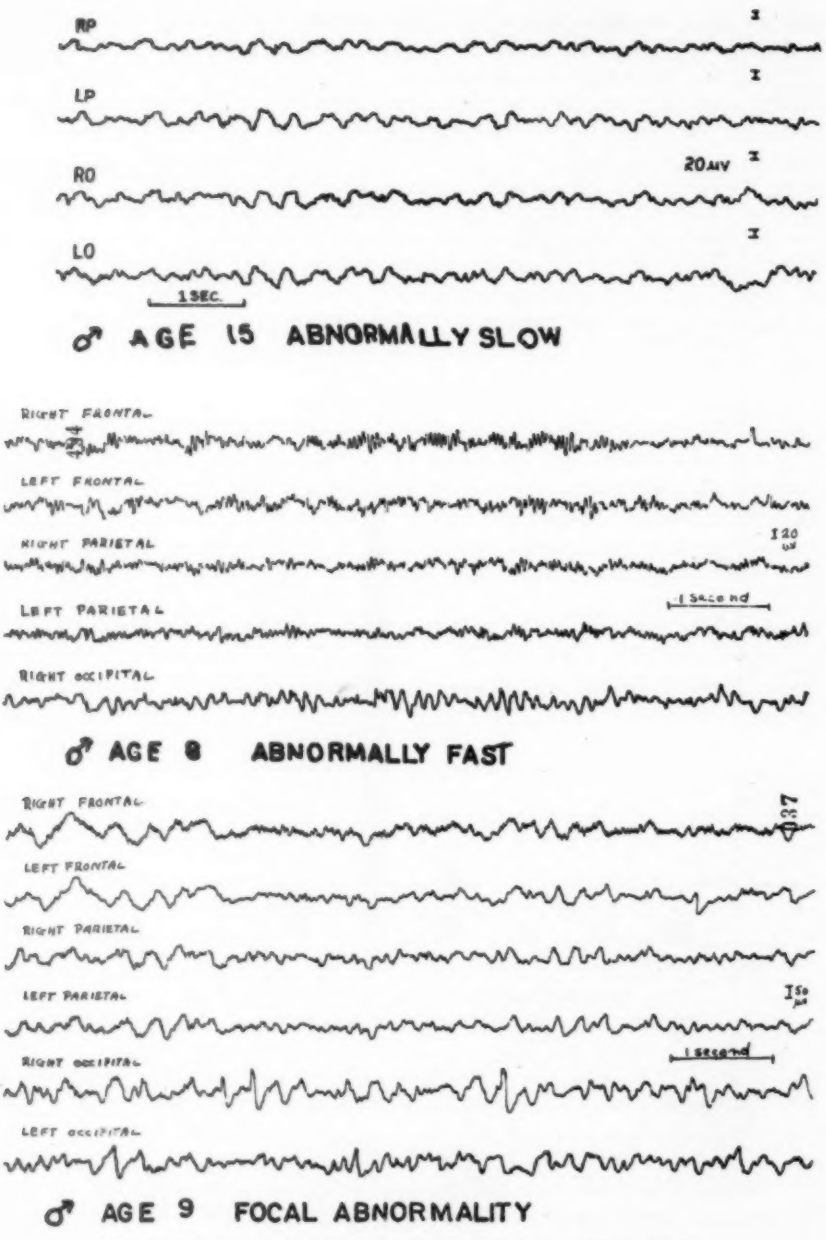

Fig. 2.—Samples of EEG abnormality in behavior problem children.

Sex Distribution.—Male patients outnumber female patients by three to one in this series. The girls have a higher percentage of EEG abnormality than the boys (Table I), but there is no marked difference in type of EEG abnormality between boys and girls.

Family History.—A positive family history (immediate relative with alcoholism, psychosis, psychopathic personality, or epilepsy) was recorded in forty-six instances. EEG abnormality is not correlated with these items in the family history in this series (Table II).

Positive Medical History.—A positive medical history (abnormal birth, head injury, illness with delirium, or high fever before the age of 2 years) was recorded in thirty-four instances. There is a slight correlation between a positive medical history, as defined, and an abnormal EEG (Table II). No item in the personal history showed a higher degree of correlation with an abnormal EEG than any other.

Neurological Examination.—Seventeen patients had positive neurological findings. These consisted of coarse choreiform movements of the extremities in fourteen, abnormal associated movements in five, hyper-reflexia in two, and nystagmus in one. These abnormalities tend to be associated with abnormality in the EEG (Table II).

Psychological Test Results.—Stanford-Binet scores in the series ranged between 58 and 140. The score was below 80 in ten and above 120 in six patients. A total of ninety-three patients had psychological examinations which were adequate to permit evaluation of possible organic factors. Thirty-two of these, or 34 per cent, had abnormal EEG's. Thirteen of the ninety-three children had psychological test results which were considered indicative of organic impairment. There is a correlation between psychological evidence of organic impairment and electroencephalographic abnormality (Table II).

TABLE II

		ELECTROENCEPHALOGRAM			
		NORMAL		ABNORMAL	
	NO.	NO.	%	NO.	%
Behavior problem children	160	144	65	56	35
Family history	160				
Positive	46	30	65	16	35
Negative	114	74	65	40	35
Personal history	160				
Positive	34	19	56	15	44
Negative	126	85	67	41	33
Neurological examination	160				
Positive	17	7	41	10	59
Negative	143	97	68	46	32
Psychological examination	93				
Organic signs	13	6	46	7	54
No organic signs	80	56	70	24	30

DISCUSSION

The present investigation confirms reports in the literature of a higher incidence of EEG abnormality in behavior problem children (35 per cent) than in normal children (10.5 per cent). The percentage of abnormality is not as high as that reported by the majority of authors, who have found 50 to 70 per

cent abnormality.[2-10] This is especially unexpected since the behavior problem children who comprise this series are not the average of behavior problems, but are children in whom the referring physician suspected "central nervous system dysrhythmia" as a factor and asked for an EEG as an aid in diagnosis.

Male patients outnumber female by three to one in this series, yet 49 per cent of the girls have an abnormal EEG as against 31 per cent of the boys. Only slight sex differences have been observed in normal children[10]—differences hardly great enough to account for the discrepancy in our series. It is probable that it takes a more severe personality disturbance to require referral of a preadolescent girl for psychiatric help than is the case with boys. This may explain the small number of girls, but it does not explain why the girls have a higher percentage of EEG abnormality unless the severity of behavior disturbance is correlated with EEG abnormality. There is no evidence in the present series which would indicate that this is so.

EEG abnormality was observed in fifty-six of the 160 children who comprise this series. The type of EEG abnormality observed in the present series was nonspecific in type and moderate in degree in thirty-three, or more than one-half of the cases. These abnormalities (moderately fast and slow) cannot be considered even suggestive of the type of pathology. Seven patients had very slow or very fast activity, which was no more specific than the moderate abnormalities but much more indicative of some type of pathology. Nine patients had slowing confined to one brain area, or spikes—abnormalities which are fairly definitely indicative of organic brain pathology in the absence of a history of seizures. Only one patient had the three-per-second spike and wave abnormality which is almost always diagnostic of epilepsy.

As to the interpretation of the EEG abnormalities, the findings in this study do not support the view that behavioral difficulties in children are related to epilepsy in the absence of overt seizures as suggested by Jasper, Solomon, and Bradley,[2] and Strauss, Rahm, and Barrera.[3] Gottlieb, Ashby, and Knott,[9] and Kennard[10] also lay stress on hereditary or "genogenic" causes for EEG (and presumably behavioral) abnormalities in these cases. The present study does not confirm the finding of a correlation between EEG abnormality and a positive family history[9] of alcoholism, psychosis, or psychopathic personality. Indeed, since these conditions are not in themselves associated with EEG abnormality in our experience, no such correlation was expected. There were too few positive family histories of epilepsy in this series to allow evaluation of this item in the family history. Patients with a personal history of convulsions were excluded from this series. The only positive correlations found in this study were between EEG abnormality and a past personal history of possible brain damage, abnormalities on neurological examination, and "organic" signs on psychological examination. It seems plain, then, that many children with behavior problems and EEG abnormality have organic brain pathology. This supports the opinion of Brill and collaborators,[5] Jenkins and Pacella,[7] and Gottlieb, Ashby, and Knott.[9] It leaves unexplained the patients with abnormal EEG's who have no evidence on the basis of history, physical examination, or psychological test of organic abnormality.

Except for patients with organically determined hyperactivity, impulsiveness, and distractibility, there is no reason to suspect a specific relation between the brain pathology and behavioral difficulty. "In the present state of our knowledge it is probably wise to assume that in interpreting behavior disorders an abnormal electroencephalogram is an indication of a . . . central nervous system which proves a handicap in social adjustment just as would poor vision, faulty muscular coordination, or a similar constitutional defect."[17]

Nor is there any reason to believe that an abnormal EEG implies a poor prognosis. The EEG may be of aid in that it may indicate the possibility of an organic handicap to which the patient can be helped to make an adequate adjustment. "A defeatist attitude is in no sense justified merely because of evidence of electrocortical dysfunction. . . .It is possible that EEG may become a valuable aid in determining or recognizing many of these handicapped personalities."[7]

The diagnosis of organic handicap cannot be made on the basis of the EEG alone, since the history and neurological examination may suggest this factor when the EEG is normal. The present study suggests that psychological testing may be a valuable addition to the diagnostic armamentarium. Unfortunately, the psychological test material available for this study was not detailed or complete enough to allow a definitive evaluation. The results are suggestive enough to warrant further investigation, and this is being carried out at present.

SUMMARY AND CONCLUSIONS

1. One hundred sixty children with behavior problems were studied electroencephalographically in the course of the diagnostic work-up. Fifty-six of these, or 35 per cent, had an abnormal EEG as contrasted with 10½ per cent in a normal group.

2. The EEG's were moderately slow or fast in thirty-three, very slow or fast in seven and slow in the occipital leads only in six. Nine patients had focal slowing or spikes, considered indicative of organic brain pathology in the absence of a history of seizures. One patient had petit mal waves.

3. Electroencephalographic abnormality does not correlate with a positive family history in this series. It does correlate with positive findings on neurological examination, a personal history of possible acquired brain pathology, and "organic" signs on psychological testing.

4. It is concluded that EEG abnormality in behavior problem children may indicate organic brain pathology. It is suggested that this organic involvement usually bears no more specific relation to the behavior disturbance than any other type of handicap.

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Case Reports

CANDIDA ALBICANS AND CRYPTOCOCCUS NEOFORMANS OCCURRING AS INFECTIVE AGENTS IN AN EIGHT-YEAR-OLD BOY

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INTRODUCTION

IT IS the purpose of this presentation to record the occurrence of *Candida albicans* and *Cryptococcus neoformans* in the same individual. Either of the fungous infections individually could have been responsible for the symptoms observed. Cutaneous infection[1] by *Candida albanicans* is common. This fungus causes other clinical manifestations which may be either localized or disseminated, acute or chronic, inflammatory or indolent, and which may affect the mucous membranes,[2] the gastrointestinal tract, the respiratory tract,[3, 4] or the central nervous system,[5–7] singly or in combination.[8, 9]

Cryptococcus neoformans also is pathogenic for man, involving more frequently the central nervous system and the lungs,[10–14] and less frequently the viscera,[15] nasopharyngeal structures, lymph nodes, muscles, bones, and skin.[16–18]

In this case the first infection observed was *Candida albicans* as proved by laboratory studies. The terminal infection with central nervous system manifestations was *Cryptococcus neoformans.*

REPORT OF CASE

B. D. R., an 8-year-old white boy, was admitted to the hospital on Jan. 23, 1945. He was emaciated and chronically ill in appearance. The chief complaint was that of diffuse, crusted, skin lesions over his face, scalp, left shoulder, fingers, and toes. The onset occurred four years prior to admission with the development of a "ringworm" type of lesion on his chin which subsequently spread over his entire head, shoulders, upper chest, and arms. These lesions cleared after x-ray and iodide therapy, only to be followed in a few weeks by a generalized eruption, from which *Candida albicans* was cultured. Later a large, dark, crusted, hornlike lesion developed over one fingernail. Gradually all but one fingernail and all of the toenails were involved by a similar process (Figs. 1 and 2). The nail and cutaneous lesions persisted as observed on admission.

The past history revealed that the patient had pneumonia at 8 months and again at 21 months of age. During the fourteen months prior to admission he had four attacks of "pneumonia," which were acute pulmonary episodes with high fever (106° F.), cough, purulent sputum production, and chest pain, lasting several days. The patient had a low-grade fever throughout his illness as well as an intermittent, slightly productive cough. Two months before admission a roentgenogram of the chest showed a large infiltrative type of lesion suggesting abscess formation in the central portion of the right lung.

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During the three years before admission six abscesses developed involving the face, left knee, and anal region. All of these drained spontaneously except the peri-anal abscess, which required incision. At the time of abscess formation the mucous membranes of the mouth and tongue became involved.

The patient lived in Kansas during the first year of his illness and then moved, with his family, to Los Angeles.

Fig. 1.—Photograph of the patient showing the skin lesions of the face, neck, and fingernails.

Fig. 2.—Photograph of the lesions of the toenails and the toes.

Admission examination.—The patient was a poorly developed, poorly nourished, chronically ill white boy of 8 years. Over the face and forehead were numerous diffuse, nonerythematous papular lesions which were covered by a rather adherent serum crust. Some of the lesions were excoriated. The same process involved the scalp, where it was associated with alopecia. These lesions averaged approximately 0.5 cm. in diameter. Over the shoulders and the left arm were larger circinate lesions from 2 to 3 cm. in diameter, with pale centers and erythematous borders. The toenails and all of the finger-

nails except that of the left index finger appeared as browish-black horns 1 to 1.5 cm. thick. There was marked clubbing of the distal phalanges. The oral mucosa, tongue, and gums were profusely covered with a white, furry mucoid covering and were hyperemic. The axillary and inguinal lymph nodes were small, shotty, and nontender. The chest was very thin with retracted interspaces. Slight dullness to percussion was noted over the entire right lung. Auscultation revealed diminished breath sounds and coarse râles both anteriorly and posteriorly over the right lung. The heart was slightly enlarged to percussion; the rate was 140 beats per minute and the rhythm was regular. The spleen was palpable 1.5 cm. below the left costal margin; the liver and kidneys were not palpable. The musculature throughout showed marked atrophy. There were no abnormal neurologic findings.

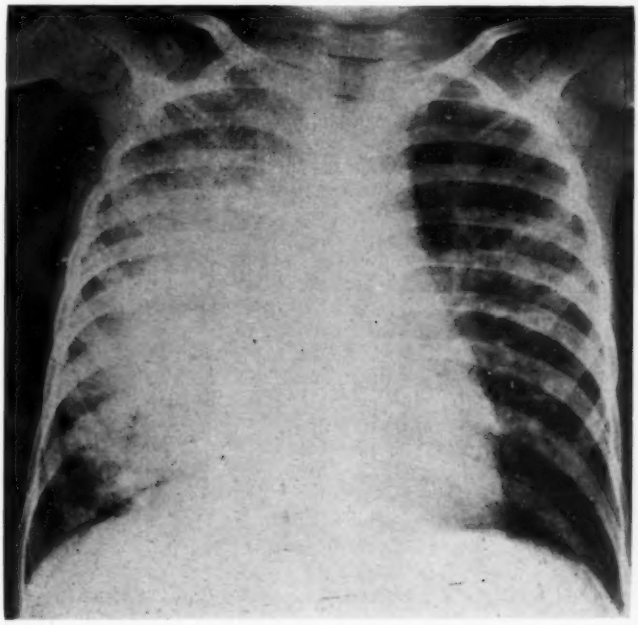

Fig. 3.—Photograph of a roentgenogram of the patient's chest taken on March 28, 1945. Bilateral soft nodular densities are seen extending outward from both hilar regions. The densities are much more pronounced on the right, involving nearly the entire lung.

Laboratory tests, including Wasserman test, were within normal limits with the exception of the erythrocyte sedimentation rate, which was 46 mm. in one hour (Westergren). There was also a slight trace of albumin in the urine. Skin tests with oidiomycin, trichophytin, coccidioidin, and tuberculin were negative. On admission blood cultures failed to show growth on blood agar, beef broth, brain broth, and on Sabouraud's medium.

Roentgenographic reports of the chest revealed soft nodular densities extending outward from both hilar regions, more pronounced on the right (Fig. 3). Roentgenograms of the long bones were negative.

Course.—The patient remained afebrile during the first week in the hospital. During the second week he began to run a septic temperature curve

daily with elevations of 104° F. Râles were heard throughout the chest and were more marked on the right. A roentgenogram taken Feb. 2, 1945, revealed the densities of the right lung to have increased. The white cell blood count rose to 16,400 per cubic millimeter with 77 per cent polymorphonuclear neutrophiles, 18 per cent lymphocytes, and 5 per cent monocytes. Blood cultures were negative. Sulfadiazine therapy was inaugurated and the patient's condition improved. The laboratory reported that cultures from the skin lesions, mouth, and sputum were positive for *Candida albicans*. The identity of the infecting organism was confirmed by sugar media reactions and by inoculation into rabbits. Following this acute pulmonary episode the patient's general condition remained stationary with a persistent low-grade fever of 101° F. Gradually there was a recurrence of leucocytosis, which ranged between 15,000 and 16,000 white blood cells per cubic millimeter with 70 to 80 per cent neutrophiles.

Forty-four days after admission an intradermal skin test was performed, using 0.1 c.c. of a 1 to 10 dilution of a heat-killed, saline suspended, autogenous, Candida antigen. No reaction occurred after forty-eight hours; a repeated dose of 0.1 c.c. of the undiluted antigen produced a zone of erythema and induration 0.5 cm. in diameter after forty-eight hours. An attempt was made to desensitize the patient to his autogenous antigen prior to specific therapy with iodides. The procedure followed a modification of the desensitization procedure outlined by Smith, Baker, and others.[19] Following the third injection of the autogenous antigen the patient had an acute exacerbation of the pulmonary symptoms. Pencillin as well as sulfadiazine was administered to combat secondary infection. The autogenous vaccine was continued until after the fifth injection, when it became apparent that the patient was in quite a critical condition. He was given two blood transfusions of 150 c.c. each. The attack gradually subsided, although the pulmonary findings remained stationary. The patient's course, following the second pneumonic episode, was gradually but continuously downhill, with weight loss, anorexia, intermittent vomiting, malaise, increasingly productive cough, and continued low-grade fever. In March, 1945, another attempt to desensitize him was begun but failed to alter the downhill course. Intravenous gentian violet and oral potassium iodide were instituted in April, 1945, after a urine culture was reported positive for *Candida albicans*.

On April 30 the patient complained of severe headache and one day later became lethargic. The spinal fluid was cloudy and under increased pressure. Cultures yielded *Candida albicans* and a roentgenogram of the chest revealed a miliary spread throughout with no apparent involvement of the pleura. Cultures of the spinal fluid and urine taken on May 3 yielded both *Candida albicans* and *Cryptococcus neoformans*. On May 5 the temperature rose to 104° F. and the patient, who had been comatose for thirty-six hours, expired.

NECROPSY

The body was that of a poorly developed, markedly emaciated white male child. The skin and nail lesions had the same appearance as on admission. The right lung, which was bound to the parietal pleura by large blanket adhesions, weighed 360 grams; the normal weight for the age group is 147 grams. The left lung weighed 360 grams; the normal weight for the age group is 152 grams. On palpation the lungs were firm and contained very little air. The lung sectioned with great resistance and the cut surface revealed large, firm, yellow and white areas from 1 to 4 mm. in diameter (Fig. 4). The tracheobronchial lymph nodes were large, measuring from 1 to 1.5 cm. in

diameter. The pulmonary mucosa was injected and roughened. Small white nodules were scattered throughout the liver. The spleen was almost twice the normal weight and contained many small white nodules throughout its pulp. The mesenteric lymph nodes were enlarged. There were also small white nodules throughout the renal tissue. The brain revealed small, firm, yellowish-white nodules averaging 1 mm. in diameter scattered profusely over the posterior parietal region and over the occipital lobes and cerebellum; occasional areas of firm white exudate were scattered over the meninges. On section the process was seen to involve only the surface of the brain. All sections of the nodules described grossly revealed the same type of lesion microscopically. These structures were composed of loose swirls of connective tissue containing transparent yeastlike cells with capsules, occasional giant cells, and epitheloidlike cells, and surrounding these cells a collar of dense fibrous tissue strands enmeshing many small round cells (Fig. 4). In some of the larger lesions, large areas of necrosis were seen. The sections of the brain showed marked vascular congestion and marked inflammatory reaction of the meninges, which were infiltrated by many polymorphonuclear neutrophiles, small round cells, and fungous cells. The cortical tissue was invaded by well-circumscribed areas in which the parenchyma was destroyed, leaving spaces containing only fine fibrillary strands of tissue in which fungous cells were seen (Fig. 5).

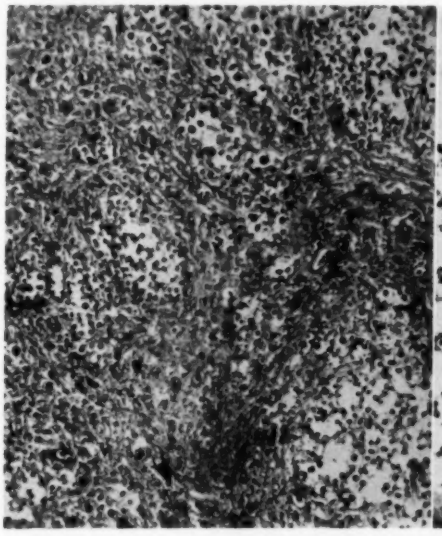

Fig. 4.

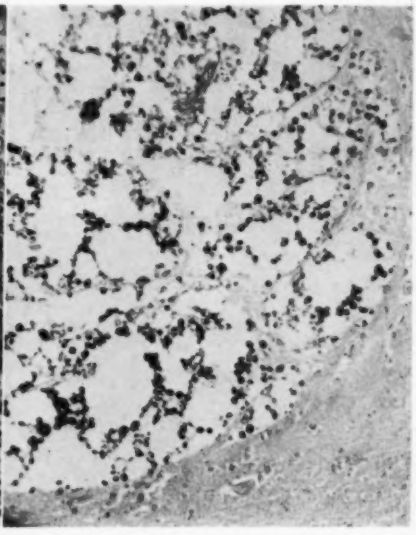

Fig. 5.

Fig. 4.—Photomicrograph of a section of the patient's lung. The alveoli are filled with many of the Cryptococcus forms as well as inflammatory cells. The alveolar walls are thickened and contain fibrous tissue strands.

Fig. 5.—Photomicrograph of a section of the cortical tissue of the patient's brain. The lesion completely destroys the brain parenchyma and the space is filled with fibrillary strands and Cryptococcus forms.

MYCOLOGY STUDIES

On the patient's admission to the hospital scrapings taken from the face, scalp, fingernails, and toenails were examined microscopically in potassium hydroxide. Candida was noted in all specimens. The sputum and scrapings

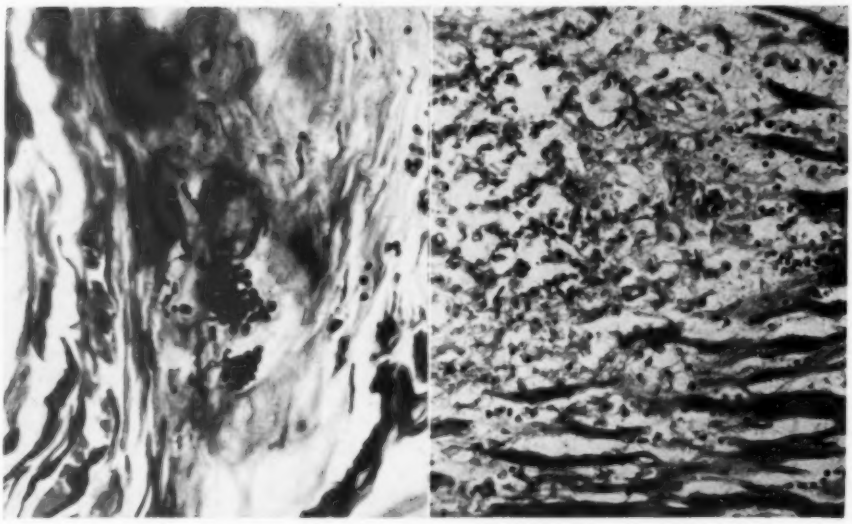

Fig. 6. Fig. 7.

Fig. 6.—Photomicrograph showing a nest of *Candida albicans* organisms in the cutaneous layers of the skin. This is from a section of a biopsy taken from the toe of the patient.

Fig. 7.—Photomicrograph showing the elongated monilial fungi in a lesion of the endocardium from a rabbit injected intravenously with a culture of *Candida albicans* from the patient. The culture was from the fingernails.

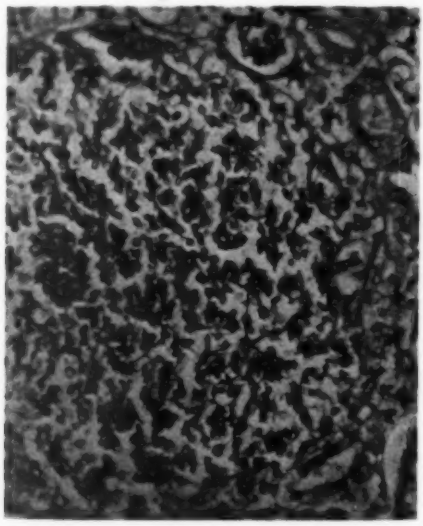

Fig. 8.—Photomicrograph showing the monilial forms in the renal tissue of the same rabbit as demonstrated in Fig. 7.

from the tongue revealed similar fungous cells. India ink mounts were also made of these specimens but no yeasts with capsules were seen. Cultures were taken from the areas listed above and these were subcultured to obtain pure colonies for classification and preparation of an autogenous antigen. A biopsy taken from a toe revealed Candida forms (Fig. 6). The mycologic studies were later repeated by the Department of Bacteriology, School of Medicine, University of Southern California. On the basis of culture, carbohydrate reactions and rabbit inoculation, both laboratories concluded that the fungus was *Candida albicans* (Figs. 7 and 8). At this time the study of the cultures appeared to be so conclusive that no additional cultures were made and attention was focussed on the treatment and clinical course. It was not until three months after the establishment of *Candida albicans* as the infecting organism, when meningitic symptoms developed, that additional cultures were taken. These cultures yielded both *Candida albicans* and *Cryptococcus neoformans*. Two hours after death cultures were taken from the blood, brain, lungs, liver, spleen, kidneys, and nails. As shown in Table I, *Candida albicans* was again recovered from the nails, spinal fluid, and urine; *Cryptococcus neoformans* was recovered from these three sites and was the only organism recovered from the brain tissue. Through an accident in the laboratory the cultures from the kidney, lung, spleen, and liver were lost.

TABLE I. ANTE-MORTEM AND POST-MORTEM MYCOLOGY STUDIES

ANTE-MORTEM MYCOLOGY STUDIES			
	CULTURES		
MATERIAL STUDIED	CANDIDA	CRYPTOCOCCUS	SECTIONS
Sputum	+		
Nails	+		
Skin	+		Candida +
Scalp	+		
Tongue	+		
Cultures 48 hours before death			
Urine	+	+	
Spinal fluid	+	+	

POST-MORTEM MYCOLOGY STUDIES			
	CULTURES		
MATERIAL STUDIED	CANDIDA	CRYPTOCOCCUS	SECTIONS
Urine	+	+	
Spinal fluid	+	+	
Brain		+	Cryptococcus +
Kidney			Cryptococcus +
Lung			Cryptococcus +
Spleen			Cryptococcus +
Liver			Cryptococcus +
Nails	+	+	Cryptococcus +
Pancreas			Cryptococcus +
Adrenals			Cryptococcus +

DISCUSSION

The patient here presented was first observed as a case of generalized cutaneous moniliasis with roentgenographic findings indicating a possible pulmonary infection. The clinical observations were confirmed by laboratory investigation, and therapy was instituted with this diagnosis in mind. The approved combination of an antigen for desensitization followed by potassium iodide therapy failed; the patient grew progressively worse, and meningitis developed.

The finding of Cryptococcus as well as Candida in the spinal fluid and urine cultures, both ante mortem and post mortem, together with the occurrence of overwhelming Cryptococcus involvement of the tissue of the brain, kidney, lung, spleen, liver, pancreas, and adrenals, brings to attention the fact that occasionally two fungous infections may exist simultaneously in the same individual. This case illustrates clearly the value of repeated frequent cultures. One must constantly be on the lookout for secondary fungi, and only by serial cultures can the time of the secondary invasion be determined. In this case the laboratory findings indicated that the primary pulmonary infection was Candida and that the Cryptococcus was superimposed terminally. The latter, however, appeared to be responsible for the death of the patient. Another assumption is that a dormant strain of Cryptococcus was present from the first along with the Candida and that it developed rapidly when the patient's resistance was depleted. On the other hand, since Cryptococcus is at times known to occur as a primary pulmonary infection before secondary invasion of the central nervous system, it is possible that the pulmonary lesion in this case was a chronic Cryptococcus infection which was not cultured because it was not possible to procure a bronchoscopic sputum specimen, and that the Candida recovered from the sputum was in the role of a saprophyte.

During the last few years the literature shows an increasing number of reports of pulmonary and systemic fungous diseases, probably because of improved diagnostic methods for recognizing these diseases. It is important that interest in this group of infections be aroused, since the pulmonary manifestations simulate the more common diseases of the lungs, and early differentiation may save the life of the patient.[3-5]

We consider the case reported here unique not only because it occured in the first decade of life[20] but because of the overwhelming secondary Cryptococcus infection occurring terminally, superimposed on a rather long-standing Candida infection.

SUMMARY

1. A case is presented of an initial chronic infection of *Candida albicans* which occurred in the first decade of life and in which an overwhelming infection by *Cryptococcus neoformans* appeared terminally.

2. The first invading organism found was *Candida albicans*. The organism was identified by clinical manifestations, by culture of morphology, by growth on differentiating carbohydrate media, and by rabbit inoculation.

3. The second organism, found only terminally, was *Cryptococcus neoformans*. Identification was obtained through clinical manifestations, cultural morphology, and carbohydrate media differentiation and animal inoculation.

The photographs are from the Department of Photography, School of Medicine, University of Southern California, at the Los Angeles County General Hospital.

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CONGENITAL DUODENAL ATRESIA

Report of a Successful Surgical Case

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THE term *atresia* signifies complete occlusion; the infant with congenital atresia of the duodenum lives but a few days unless it receives prompt surgical treatment.

This condition, recognized by Calder as early as 1733, was invariably fatal until 1916, when Ernst recorded the first successful treatment. Miller,[3] in 1939, and Ward and Cooper,[5] in 1943, each reviewed the literature, carefully tabulated the successful cases, and added successes of his own. Later Kautz and co-workers[2] surveyed the literature concerning congenital duodenal obstructions in general from the viewpoint of the roentgenologist. In 1945 Sumner and Morris[4] described the case of a patient whom they had treated successfully and whom they believed to be the sixteenth reported survivor.

During the thirty-two years since Ernst's case was published the surgical techniques of dealing with these infants have been greatly improved, largely through the efforts of Ladd, Donovan, Miller, and a few others. Yet today medical literature records the six-month survival of fewer than thirty such patients.

It is difficult to gauge the incidence of this anomaly, but the condition is probably much more common than is generally realized. From figures presented by Davis and Poynter[1] a quarter of a century ago, we may deduce that congenital atresia of the duodenum occurs once in approximately 58,500 live births, and Kautz and co-workers[2] recently asserted that only about 300 cases have been recorded.

The most obvious symptom is persistent vomiting, usually beginning with the first feeding. Dehydration is rapid, and death commonly occurs during the first week; there is no record of survival beyond the twelfth day without surgical intervention. Exact diagnosis depends upon roentgenologic study of the intestinal tract: absence of gas in the lower intestinal tract indicates atresia, and failure of barium to pass through the duodenum after six hours definitely localizes the occlusion. Such study should be instituted promptly whenever clinical observation or history suggests the possibility of atresia. Alertness to that which is too often dismissed as a trivial symptom and promptness in determining its cause offer the only hope of life to these little patients.

CASE REPORT

A white female infant was brought to us at the age of 10 days with the complaint of having vomited after each feeding since birth.

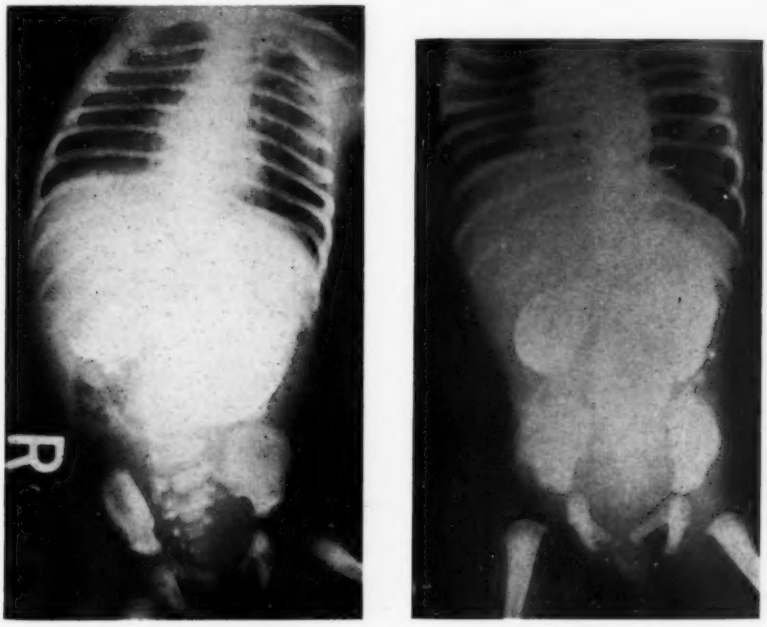
History.—The patient's birth weight was 6 pounds, 8 ounces. She had been treated by the administration of subcutaneous fluids. To the best of the parents' knowledge no yellow stoools had as yet been passed. The family history was noncontributory; one brother and two sisters were living and well.

Examination.—The patient weighed 4 pounds, 15 ounces, representing a weight loss of more than 1½ pounds since birth. A moderate degree of jaundice existed. Upon rectal examination a small amount of bile-stained meconium was obtained; no cornified epithelial cells were found in this meconium. The abdomen was not distended and no pyloric tumor was palpable. The infant was

immediately subjected to roentgenologic study. Plain films revealed an absence of gas in the lower intestine; therefore, barium was administered orally and roentgenograms were made at one, four and one-half, and sixteen hours. The duodenal cap filled easily and showed distention, but no barium left the first portion of the duodenum in sixteen hours.

Treatment.—Preoperative care consisted chiefly of the administration of physiologic saline solution by the subcutaneous route and Synkamin intramuscularly. Gastric lavage preceded surgery.

Through an incision extending from the ensiform to the umbilicus the presence of duodenal atresia was confirmed. After determining that there were no other anomalies present in the intestinal tract, an isoperistaltic posterior gastroenterostomy was accomplished, under open cone ether anesthesia, twenty-four hours after we first saw the patient.



A. *B.*

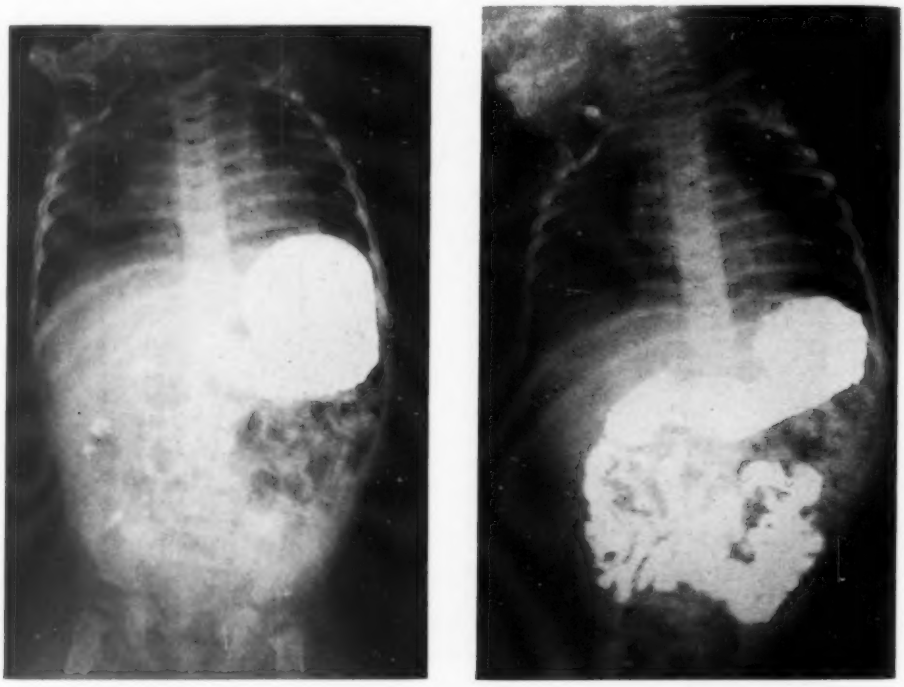
Fig. 1*A*.—Preoperative barium study one hour after oral administration of barium, showing filling and distention of duodenal cap.

Fig. 1*B*.—Preoperative barium study sixteen hours after oral administration of barium, showing complete failure of the contrast medium to pass beyond the duodenum.

Immediately after the operation hypodermoclysis of physiologic saline solution was begun. Boiled water was offered at three-hour intervals and approximately one-half of it was retained. The infant was put on a low-fat formula nineteen hours postoperatively. Early on the second postoperative day parenteral administration of glucose in saline was begun and repeated twice daily until the fifth day, when the patient was put on a regular formula and the daily administration of Zymadrop begun. On the tenth postoperative day ascorbic acid and Drisdol were added to the diet. Pablum was begun ten days later.

Results.—There was a slight but constant gain in weight from the beginning of treatment onward. When discharged, twenty-six days after operation, the infant weighed 6 pounds, 15½ ounces, and was accepting 4 ounces of formula at normal intervals.

At 3 months of age the child was started on beef and liver soup, potato, strained vegetables, jello, and similar foods.



A. *B.*

Fig. 2*A*.—Postoperative barium study of same infant six months later, thirty minutes after oral administration of barium.

Fig. 2*B*.—Ninety minutes after oral administration of barium, demonstrating functioning anastomosis and normal passage of the contrast medium.

When the patient was 6 months old another barium study was made. X-rays taken at intervals of thirty minutes, one hour, ninety minutes, two hours, and three hours showed the stomach to be emptying satisfactorily. There had been no vomiting since discharge from the hospital. Weight was 14½ pounds, length 25½ inches, head 16¼ inches, and chest 15½ inches at that time. She was then put on a three-meal regime, and her progress continued to be entirely satisfactory when last seen, at the age of 9 months.

SUMMARY

Congenital duodenal atresia is an urgent surgical condition of the newborn. Fewer than thirty six-month survivals have been recorded to date. Appearance of the most obvious symptom, persistent vomiting after feeding, justifies immediate roentgenologic study.

We have reported the case of an infant first seen by us at the age of 10 days and successfully treated by posterior gastroenterostomy.

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NEONATAL ASPHYXIA DUE TO BRANCHIAL CLEFT CYST

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WARREN S. WILKINS, M.D.
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NEONATAL cyanosis and respiratory embarrassment are associated most commonly with such conditions as difficult or instrumental labor, use of prenatal analgesics or anesthetics in the mother, atelectasis, aspiration of amniotic fluid, cerebral birth injury, and prematurity. Yet occasionally tumors and cysts, often in obscure locations, may obstruct the airways and thereby lead to asphyxia and/or death.[1, 2] Therefore, it is important to search for possible obstructive masses in infants exhibiting neonatal respiratory distress. We wish to present a case of an infant with neonatal asphyxia due to a branchial cleft cyst.

CASE REPORT

C. R., a 7-day-old female infant, was admitted to Freedmen's Hospital May 12, 1947, because of respiratory difficulty present since birth. The family history was noncontributory and the prenatal period was essentially uneventful. Birth occurred May 4, 1947, at another hospital after a full-term gestation. Labor was uncomplicated and lasted four hours. The infant breathed spontaneously at birth and weighed 5½ pounds. Between May 4 and May 8 the infant developed respiratory difficulty. There was inspiratory retraction of the lower end of the sternum. Intermittent cyanosis of the lips, palms, and soles was observed, particularly after feeding. Respirations were noisy and crowing in character and on the day of admission they became rapid. The infant salivated constantly. She appeared to swallow with difficulty and regurgitated frequently during and after feeding. The vomiting was not forceful and vomitus consisted of curdled milk and mucus. The appetite remained good and the infant had a strong sucking reflex. Stools were normal. There were no convulsions.

Physical examination disclosed a poorly nourished, dehydrated, Negro female infant, weighing 5 pounds, 4 ounces. She was active and vigorous. The skin was dry and peeling over the feet, trunk, and arms. The palms and soles were pink. The head, scalp, fontanelles, and ears were negative. The nose, mouth, and pharynx contained a large amount of thick, tenacious mucus. Digital examination of the base of the tongue revealed no palpable tumor masses. The cry was staccato and hoarse. Inspiration was accompanied by marked retraction of the lower end of the sternum and a hoarse stridor. These findings were reduced on sleeping and quiet breathing. The infant appeared more comfortable in the prone position; breathing was easier, less labored, and less noisy. The examination of the heart, lungs, and abdomen was essentially negative.

Under fluoroscopy a soft rubber catheter passed without obstruction through the esophagus into the stomach. An admission roentgenogram of the chest revealed clear lungs, a normal cardiac silhouette, and no mediastinal widening. The admitting diagnosis was laryngeal obstruction of unknown etiology.

The hemogram showed 12,750 white cells and 5.5 million red cells per cubic mm. The hemoglobin was 14.5 Gm. per cent. The blood Kahn was negative.

From the Division of Pediatrics and the Department of Pathology, Howard University School of Medicine and Freedmen's Hospital.

Immediate treatment included oxygen, prone position, intermittent steam inhalations, parenteral fluids, supplementary vitamins, and frequent small feedings. These measures were continued throughout the hospital course.

On May 13 the infant was examined by the consulting otolaryngologist who found nothing of significance. He suggested irradiation of the thymus gland and direct laryngoscopy if no improvement ensued. By May 16 the infant's condition was thought to be improved. Secretions from the nose and throat had diminished and respirations were quieter. However, she continued to exhibit episodes of stridor and costal retraction alternating with periods of quiet normal breathing. Additional therapeutic measures instituted at this time included penicillin, ephedrine sulfate nose drops, and feeding by gavage. Since only periodic improvement in the patient's condition had been noted, on May 22 direct laryngoscopy was done. Direct vision of the epiglottis, larynx, vocal cords, and arytenoids showed no abnormality.

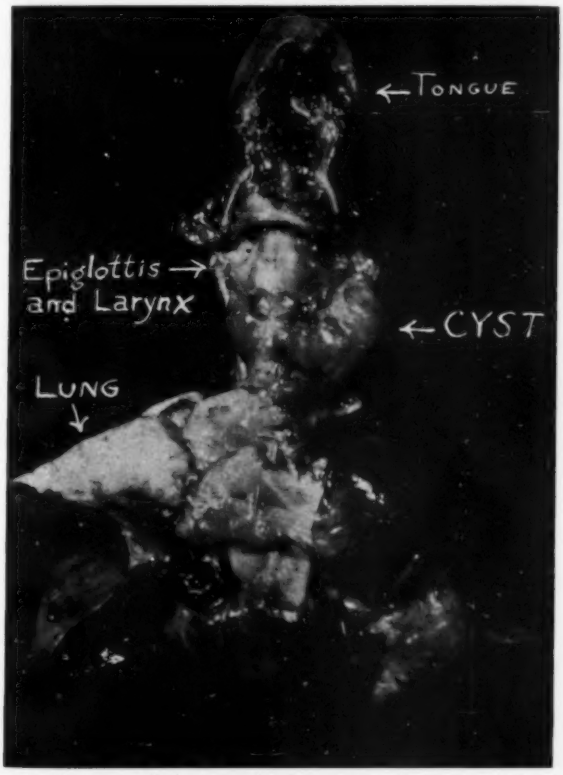

Fig. 1.—Photograph of gross pathologic specimen removed at autopsy demonstrating the cyst in intimate relationship with laryngeal and pharyngeal structures.

The clinical picture continued as before with periodic attacks of stridor and retraction of the thoracic cage alternating with intervals of quiet breathing. The infant was afebrile during the entire hospital course. Repeat roentgenograms of the chest on May 21 and May 27 were negative. The infant expired May 27.

Post-mortem examination of the infant immediately after death revealed a cystic mass in the anterior triangle of the neck on the left side. It was moderately firm, movable, and clearly transilluminated. The inner wall of the mass bulged into the oropharynx as a soft cystic swelling capable of obstructing both larynx and esophagus. Dissection of the neck and thorax exposed a cyst which was situated just posterior and lateral to the upper end of the esophagus. The cyst was soft, thin-walled, and measured 4 by 1.3 by 2.5 cm. The medial wall of the mass was in intimate contact with and covered the cricothyroid muscle and the left anterolateral surface of the larynx. The cyst extended posteriorly and caudally to compress the pharynx, esophagus, and trachea. The left lateral lobe of the thyroid gland was compressed by the cystic structure whose contents consisted of soft cheesy material (see Fig. 1). There were no significant gross findings in the other visceral organs.

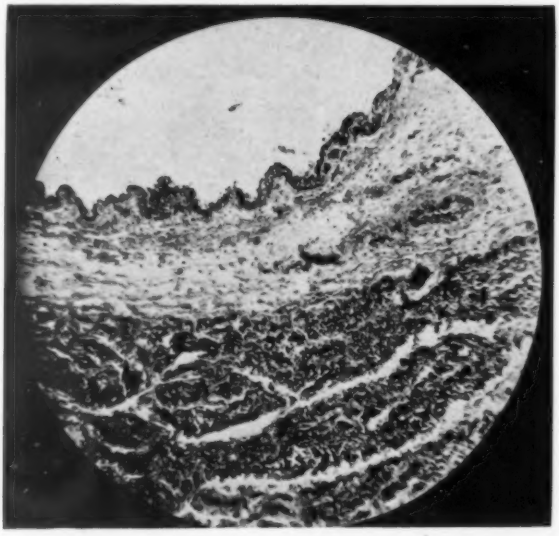

Fig. 2.—Photomicrograph of section made through the cyst wall showing stratified squamous epithelium lining, connective tissue stroma, and adjacent thyroid tissue adherent to the cyst wall.

Microscopic Examination.—The cyst was lined by stratified squamous epithelium (see Fig. 2). Sections of the liver showed fatty metamorphosis, immature red blood cells in the sinusoids, and phagocytosed pigment in macrophages. The lungs exhibited patchy emphysema, alveolar and interstitial hemorrhages, edema, and scattered atelectasis. The kidneys showed cloudy swelling and hemorrhages into Bowman's capsule. Sections of the adrenal glands revealed medullary hemorrhages. The pathologic diagnosis was asphyxia caused by a left branchial cleft cyst which compressed the larynx, trachea, pharynx, esophagus, and left lobe of the thyroid gland.

DISCUSSION

Branchial cleft cysts and fistulas often do not manifest themselves in early childhood.[3, 4] Most reports in the literature concern cases in adults and children past infancy.[4-7] Baumbartner[3] in 1933 reviewed the records of the Chil-

dren's Hospital of Los Angeles and found only four cases of branchial cleft cysts and fistulae, only one of which was apparent at birth. Hyndman and Light,[8] in reviewing ninety cases, noted that the average age of onset was 17 years. The condition was noticed at birth in 21 per cent of the cases and in only 11 instances was the cyst diagnosed before 11 years of age.

The usual symptoms produced are the presence of a uniform, painless, semifixed, fluctuant, cystic tumor in the neck, and a persistent discharge in the case of fistula. If infection takes place, the symptoms of inflammation, acute or chronic, develop. Occasionally, pain due to local pressure may be present. In the absence of infection such cysts and fistulas usually produce no great discomfort.[3, 8]

Less commonly, unusual symptoms may be produced. Thomson[9] reported a case in an adult associated with local pain, husky voice, fixation of the vocal cord, and dyspnea. At operation the cyst was found attached to the left lamella of the larynx and greater cornu of the hyoid and passed inward to the lateral wall of the pharynx. Removal of the cyst relieved all symptoms.

Carp[10] presented a case of a fistula accompanied by an unproductive cough of two years' duration. The fistulous tract was found attached to the vagus nerve. Extirpation of the fistulous tract led to relief of the cough. Similar symptoms of vagal stimulation such as nervousness, restlessness, hoarseness, palpitation, vomiting, pallor, and intermittent pulse may follow probing, pinching, or distention of the fistulous tract.

Smith[11] described a fistula in a 3-week-old child whose respiration and deglutition were markedly impaired.

In our case the inner wall of the cyst at times prolapsed over the upper aperture of the larynx and compressed the trachea and esophagus, leading to stridor, obstruction to deglutition and respiration, and eventually to death from asphyxia.

SUMMARY

A case of neonatal asphyxia due to a branchial cleft cyst is presented along with a review of the usual and unusual symptoms accompanying such cyst.

The authors wish to acknowledge the assistance of Dr. John F. G. Clark in the preparation of the pathology report.

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Clinical Conference

CONFERENCE AT THE UNIVERSITY OF ARKANSAS HOSPITAL

WILLIAM A. REILLY, PROFESSOR AND HEAD OF PEDIATRICS

Case 1. Tuberculous Caseous Pneumonia

DR. HAROLD MILLER (Assistant Resident in Pediatrics).—J. L., an 8-month-old white girl, was admitted March 5, 1948, with a history of seeming well until two months before admission, when she developed fever, cough, vomiting, and some respiratory difficulty. There was anorexia and irritability associated with a weight loss of about 3 pounds. The infant's grandfather had died of tuberculosis one year previously and she had been exposed frequently for the past six months to an aunt who had active tuberculosis which was discovered three months prior to admission.

The patient appeared quite ill; rectal temperature was 102.4° F.; the skin of the abdomen was loose; the chest revealed marked dullness on percussion over the entire left lung, sibilant and crepitant râles over both lung fields, and bronchial and amphoric breathing in the left axilla; a firm spleen was palpable about one inch below the costal margin.

The Mantoux test with 0.1 mg. of old tuberculin was positive with a 2.5 cm. area of induration and erythema. Spinal fluid findings were normal, including culture for tubercle bacilli. A chest film (Fig. 1 revealed a multiloculated cavity involving the midportion of the left lung and extending into the hilus, with a diffuse infiltration surrounding the cavity and a widening of the superior mediastinum; the right lung field was clear. Gastric washings showed the presence of acid-fast bacilli.

Streptomycin was administered intramuscularly from March 13 to May 19, 1948, in a dose of 320 mg. daily (25 mg. per pound of body weight) divided into four parts and given every six hours. A total of 21 Gm. was thus administered.

The temperature began to fall from 103° F. daily after the first week of treatment to about 100.6° F. maximum daily, and after the third week remained normal; weight began to increase after the fourth week.

Chest films after three weeks of therapy showed the right lung to be clear with the left lung showing considerable regression in the size of the cavity and the area of involvement, but widening of the superior mediastinum was still present. A film taken forty days after starting streptomycin showed still further diminution in the size of the cavity and also in the width of the superior mediastinum.

Treatment was to be continued at home after May 19, 1948, but was not given. She entered a sanatorium on June 21, 1948. In the next two months she progressed favorably, gained 2½ pounds, remained afebrile, and by the end of September seemed to be quite well. At this time the chest film showed no evidence of residual involvement as compared to a chest film taken on June 21,

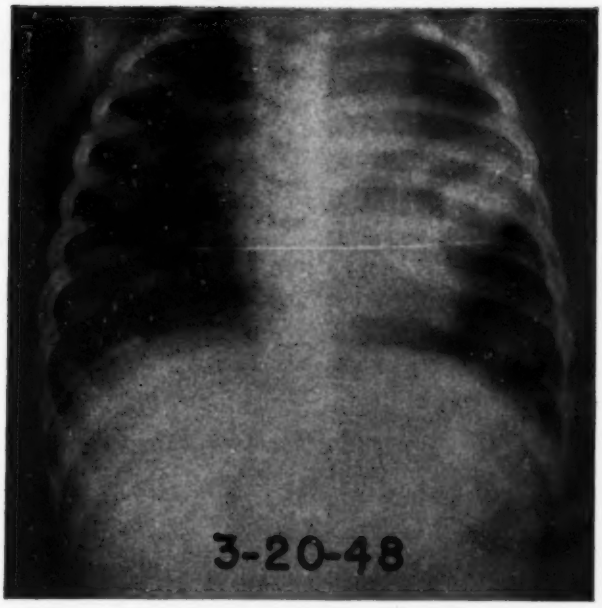

Fig. 1.—Case 1. Tuberculous caseous pneumonia with cavity.

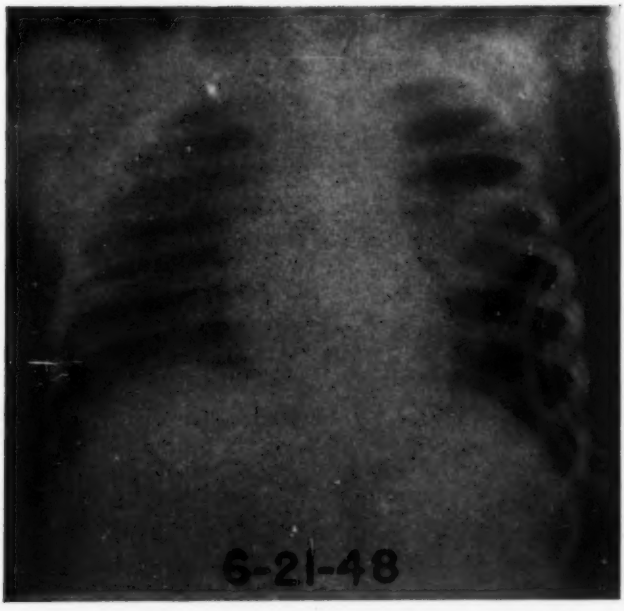

Fig 2.—Case 1. Cavity had diminished considerably three weeks after starting streptomycin. This picture taken three months later did not show a cavity but only slight residual involvement of the left lung. After another three months the lungs were normal roentgenologically.

1948 (Fig. 2) which showed regression of the left superior mediastinal lymph nodes and of the area of involvement adjoining the left hilus. A cavity could no longer be identified.

DR. WILLIAM P. BARRON (Assistant Resident in Pediatrics).—Did streptomycin arrest the disease process?

DR. REILLY.—At this age a spontaneous recovery from this type of tuberculosis is rare. The disease usually terminates fatally. In this case, clinical improvement was apparent shortly after therapy was begun. No dissemination occurred. We feel that streptomycin was responsible for the retrogression of the tuberculous process.

DR. VIDA GORDON (Associate Professor of Pediatrics).—Was the duration of treatment sufficient?

DR. REILLY.—In view of knowledge at that time, it would have been advisable to continue therapy for another three to four months. There are several others who have successfully treated this caseous type.[1, 2] Unknown to us, therapy was not continued at home as previously arranged.

A brief survey of our results (Table I) with various types of tuberculosis shows that streptomycin has been helpful in four of the seven cases. We have treated others but started too late. P. A. had a tuberculous meningitis which, during three months of therapy, had not progressed clinically. The child has been free of fever, somnulence, weight loss, anorexia, and the other usual evidences of toxicity; frequently she sits and plays; however, there is tremor of the extremities, possibly due to the medication as well as the disease; nuchal

TABLE I. TUBERCULOSIS TREATED WITH STREPTOMYCIN

NAME	AGE	TYPE	DURATION OF DISEASE	DURATION OF THERAPY	TOTAL DOSAGE (50-80 MG. PER KG. PER DAY)	RESULT
1. J. L.	8 mo.	Pulmonary with cavitation	2 mo.	2½ mo.	21 Gm. IM.*	Improvement clinically x-ray findings not completely cleared.
2. R. D.	5 mo.	Meningitis pulmonary with possible cavitation	8 days	2 mo.	20.6 Gm. IT.† and 0.8 Gm. IM.	No improvement; spastic; died a few days after discharge.
3. C. B.	4 mo.	Meningitis and pulmonary	5 weeks	1 mo.	46.6 Gm. IM. and 1.1 Gm. IT.	No improvement.
4. S. H.	4 yr.	Lymphadenitis	6 mo.	3½ weeks	12 Gm. IM.	Marked improvement.
5. W. W.	4 yr.	Meningitis and pulmonary	4 mo.	5 weeks	30.2 Gm. IM. and 0.85 Gm. IT.	No improvement.
6. J. S.	13 mo.	Meningitis and pulmonary	3 weeks	2½ mo.	179.4 Gm. IM. and 0.73 Gm. IT.	Improved
			6 mo.	5 weeks	43.1 Gm. IM. and 0.435 Gm. IT.	No improvement; spastic.
7. P. A.	16 mo.	Meningitis and possible pulmonary	2 weeks	2 mo.	23.6 Gm. IM. and 1.750 Gm. IT.	Improved; still receiving therapy.

*IM. = Intramuscular.
†IT. = Intrathecally.

rigidity is ever-present; the spleen is palpable, and there has been possible pulmonary involvement. The toxicity, the draining abscess, and biopsy incision in S. H. receded and healed very favorably—much more quickly than during a regime used for six months before streptomycin. The patient may have developed some immunity before streptomycin was started; the antibiotic may have stopped the growth of the tubercle bacilli and thus further aided the patient. J. S. showed improvement after the first course of therapy, but after two months without therapy there was still some evidence of meningitis and spasticity had developed. A second course of five weeks of therapy was given with no improvement and death occurred eight days later.

The other three patients have not responded to this therapy, usually because of the previous duration and dissemination of the tuberculosis.

Case 2. Pertussis Pneumonia

DR. ALICE GAMBLE (Instructor of Pediatrics).—L. M., a 2-month-old Negro female infant, was admitted March 11, 1948, with the chief complaint of continuous paroxysmal coughing. Aside from a mild cold, the baby had been well until six days before admission, at which time a mild temperature elevation, rhinitis, and respiratory difficulty were noticed. Three days before admission the paroxysms of coughing became more frequent and productive of white phlegm. Cyanosis was present during the paroxysms.

On admission the child was acutely ill with paroxysms of coughing every few minutes associated with cyanosis. The respiratory rate was rapid and grunting in character. The weight was 3.3 kg.; pulse, 148; temperature, 99.4° F.; and respiration, 96.

Pertinent physical findings included dilatation of the alae nasi and crepitant, vesicular râles over the right lung fields with impaired resonance over this area, which lead to a diagnosis of right bronchopneumonia. The chest film confirmed this diagnosis. Although four cough plates were taken, only the first yielded a Hemophilus organism not definitely identified as *Hemophilus pertussis*. The leucocytes ranged in number from 46 to 67 thousand with 79 to 84 per cent lymphocytes.

This child was given 200 mg. of streptomycin daily in doses of 25 mg. every three hours for eight days (approximately 75 mg. per kilogram daily). In addition, sulfadiazine, oxygen, and sedation were used. Although early the child had twelve to fifteen paroxysms daily; on the fifth day on streptomycin only four mild paroxysms were charted. The streptomycin was discontinued on the eighth hospital day and the patient was discharged two weeks after admission. Her outpatient clinic follow-up revealed an uncomplicated convalescence as manifested by weight gain and disappearance of paroxysms.

DR. GORDON.—Streptomycin alone or combined with sulfadiazine is being used effectively in several parts of the country for whooping cough. We have admitted eleven patients with severe pertussis since January, 1948, all of whom received streptomycin in doses of 50 to 75 mg. per kilogram daily. All of these patients (except one who was moribund at admission) were noticeably improved

within a period of two to five days after beginning streptomycin. In some cases the response was most dramatic in that hard paroxysms would cease in eighteen to twenty-four hours after treatment began. In the case reviewed the prognosis would previously have been poor because of the pneumonia complicating pertussis in a 2-month-old infant. Bradford[3] and Hegarty[4] as early as 1945 demonstrated the bacteriostatic and bacteriocidal effect of streptomycin on mice infected with *H. pertussis* and suggested clinical trials. By clinical evaluation we have felt that their recommendation was warranted.

DR. REILLY.—The question of inherited immunity and placental transfer of antibodies in pertussis is illustrated in another case of a newborn infant whose mother was exposed to whooping cough shortly before delivery. At the time of delivery the mother was having paroxysms of coughing even though she had a history of having had whooping cough as a child. Two weeks after delivery the baby began having typical paroxysms of coughing with vomiting, though she had not been in contact with the infected children. She had an admission leucocytosis of 25,750, 60 per cent of which were lymphocytes. Even though a cough plate did not yield *H. pertussis*, we felt this was a case of either pertussis or parapertussis.

Kendrick[5] has shown that even in mothers who have had pertussis in childhood, the amount of circulating antibody during adulthood is low and the amount transferred to the fetus even lower. By immunization with pertussis vaccine during pregnancy the effective protection in both the mother and child is raised. In mothers who are pregnant during the winter months and who have large families, it would seem that immunization of the mothers during the last trimester of pregnancy would help protect the infants during the first crucial months of life until active immunization could be started at 2 to 3 months of age as suggested by Di Saint Agnese and Sako. Christie and Peterson showed that such young infants generate pertussis antibodies.

Case 3. Cutaneous Anthrax

DR. EUGENE CRAWLEY (Instructor of Pediatrics).—A 15-year-old boy skinned a steer which died of what later was proved to be anthrax by the state veterinarian. There were thirty head of cattle that died from anthrax in this area during the months of September and October. On October 12, the patient noticed a small vesicular lesion on this right forearm on the volar surface. By October 13, this lesion had become very dark and there was marked swelling for several inches around the dark center. There was regional adenopathy. That night the patient began to have high fever and felt very ill. The patient was admitted on October 16 with a diagnosis of anthrax by his local physician. Smears and cultures for anthrax and agglutinations for tularemia were negative. The principal findings on admission appeared to be typical of anthrax and there were malignant pustules, malignant edema, and right axillary lymphadenopathy. Temperature was 99.6° F., pulse 120, respiration 20. The patient has a pre-existing and apparently unrelated chronic glomerulonephritis. In

view of the renal pathology which could be complicated by sulfonamide therapy and on the basis of successful eradication of anthrax in animals by streptomycin, it was decided to treat this patient with streptomycin. Within twenty-four hours following the initial dose intramuscularly of 500 mg. the patient was improved and 250 mg. were given every three hours for five days until the patient was markedly improved. The edema had almost disappeared and slight fever continued only twelve hours longer. The axillary lymphadenopathy had disappeared on October 22. The patient was discharged on the tenth hospital day with a dry, desquamating area, 3 cm. across, having a small eschar thereon.

DR. REILLY.—This boy acquired anthrax at the same time and in the same area as four adults whom we proved by smear and culture to have cutaneous anthrax. Three of the adults had skinned a diseased cow; the fourth adult's only contact was by dressing her husband's lesions. This is the first known human-to-human acquisition. The adults quickly recovered within two to five days with daily doses for five days of 300,000 to 400,000 units of penicillin and 6 Gm. of sulfadiazine. Smaller doses of penicillin for shorter times (seventy-two hours) have resulted in cures and negative cultures by the second to fifth day (Murphy[6]). Miller[7] showed that 93 per cent of mice infected with anthrax survived when adequately treated with streptomycin for seven days, 58 per cent survived with penicillin for seven days and 5 per cent with sulfadiazine for seven days. Culturally streptomycin prevents the growth of the anthrax baccilus. Our sensitivity tests with the anthrax cultures from the adults showed that streptomycin was far more effective than penicillin. We felt, but did not prove, that the boy had a septicemia; there was no evidence of a pulmonic form. This is the first record of human anthrax treated with streptomycin.

DR. GAMBLE.—It is possible that the virulence of this anthrax was not great enough to cause a septicemia form in the human, but did so in the cattle. In septicemic cases perhaps it would be best to use all of these antibiotics. Gold[8] stated that sulfathiazole is the most effective of the sulfonamides.

Case 4. Osteopetrosis

DR. J. A. HARREL, JR. (Assistant Resident in Pediatrics).—D. S., a white boy 15 years, 10 months old, was admitted to the hospital with chief complaint of drainage and pain in both ears, which had been present since he was 6 years of age. Whenever the drainage ceased, the patient would have severe headaches and diminished hearing. The father had noticed some abnormality of the growth of the child's head and mandible for three or four years, but no other abnormality in the skeleton. The child did not attend school because of slow mental development. The patient has never had any fractures.

The family consisted of the father, 38 years old; mother, 44 years old; and five brothers between 5 and 20 years of age. Hereditary diseases, similar complaints, and consanguinity were denied.

The patient was 70 inches tall, his span was 64½ inches, lower (from symphysis to heel) was 36 inches, skull 23½ inches circumference (average is 22½ inches). The nasal bridge was thickened laterally and very shallow. The

mandible was greatly and regularly thickened. The palate was very high and narrow, the orbits were widely separated (ocular hypertelorism), and there was mild exophthalmos present. There was thick, foul-smelling pus filling the left auditory canal and there was a large perforation of the left eardrum. There was also a perforation of the right eardrum with no drainage present. There was normal dental development for the age but marked malposition of teeth and overgrowth of the gingiva. Chest, heart, and abdominal examinations were negative. Genital development was slightly retarded for the age and there was no axillary hair. Skeletal examination revealed uniform thickening of the ulna and radius, clavicles, femora, and the lower one-third of both tibias. Neurological examination was essentially negative except for slight edema of the nasal sides of both optic nerve heads.

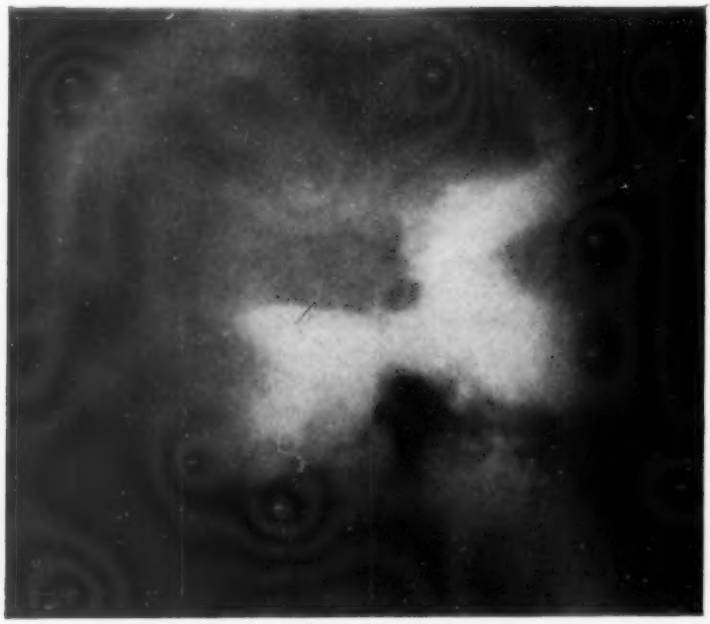

Fig. 3.—Case 4. Osteopetrosis. Note the great thickness and density of all of the skull and facial bones.

Laboratory examinations revealed normal red and white count, adequate hemoglobin and normal differential. The following were the findings in 100 c.c. of blood, with normal values in parenthesis: calcium 11.5 Gm. (9 to 11.5), phosphorus 5.2 mg. (4 to 7.1), alkaline phosphatase 34.5 King-Armstrong units (3 to 13). Serology revealed a negative Kahn. Spinal fluid examination revealed normal findings for the following: pressure, cell count, protein, and sugar. Gum mastic curve and Kolmer test were negative.

DR. I. MESCHAN (Professor of Radiology).—Routine films of the skull (Fig. 3) and special films of the mandible show a marked sclerosis of all of the bones at the base of the skull and mandible and widening of the diploe of the calvarium, which measures as much as 2½ cm. in thickness. The air spaces of the sinuses are completely obliterated and the clinoids are markedly sclerotic. The bones of the mandible are widened and sclerotic but the teeth appear to be normal. There is no calcium deposit in the pineal gland. The bones are so densely sclerotic throughout the face and skull that all detail is obscured.

Fig. 4.—Case 4. Osteopetrosis. Diffuse osteosclerosis of cortices and obliteration of medullary cavities.

Anteroposterior films of the ribs and shoulder girdles show a similar marked sclerosis of all the bones of this region. The shaft of the clavicle is widened. Anteroposterior views of the hands, feet, and forearms show a marked sclerosis of the shafts of these bones with considerable endosteal bony proliferation. The long bones are spindle-shaped as a result of this sclerosis, but the carpal and tarsal bones are little involved.

In the legs there is complete obliteration of the medullary portion of the bone by sclerosis with little change in the metaphysis and epiphysis. Anteroposterior and lateral views of the lumbar spine and pelvis show a similar sclerosis of the vertebral bodies and bones of the pelvis. They have a somewhat doubled contour appearance suggesting arrested development at some time in the past. The epiphyses are relatively uninvolved and their age equals the chronological, except for one area which is at the twelve-year age level.

There is diffuse osteosclerosis of all the bones of the body, effecting those of the shoulders, mandible, skull, metaphysis and diaphyses of the long bones predominately. I would consider the most likely diagnosis to be osteopetrosis (Albers-Schönberg disease). Against this is the marked effect on the calvarium proper and the absence of club-shaped long bones. Fluorine poisoning must also be excluded. The vertebrae resemble phosphorus poisoning but the rest of the skeleton does not fit this diagnosis. Paget's disease does not fit the appearance of the long bones and leontiasis ossea likewise cannot be fitted into the appearance below the skull, since this entity is probably a variety of osteitis fibrosa cystica.

MR. LOWELL OZMENT.—Leontiasis ossea and generalized Paget's disease were ruled out; at entry his face strongly suggested acromegaly. He was eunuchoid in proportions and had delayed sexual development.

DR. REILLY.—The chief features of the syndrome are abnormal density of the bones with or without fragility, a strong tendency to anemia which may be severe and fatal, and optic atrophy. There is a distinct familial tendency and the disease is occasionally inherited. It affects all ages and sexes, male individuals slightly more frequently than female. The etiology is unknown. The affliction may be benign or malignant; there may be intermissions, remissions, or complete cessation of the developmental error. As a rule the bones are very hard like marble but soft bones have been reported. Fragility has been exaggerated in the literature. Anemia is usually present, due to the reduction of the blood-forming marrow in the sclerosed bones. The anemia is usually a source of real danger but it by no means corresponds always to the severity of the disease. Serum calcium is usually normal; plasma phosphatase is either normal or slightly low. Optic atrophy may result from thickening about the optic foramina. Nystagmus, hydrocephalus and deafness are other not very uncommon complications. The teeth are prone to decay.

The primary cause of this type of osteoclerosis is a reduction in osteoclastic resorption so that there is a failure in timing of bone apposition and resorption. Investigations of calcium and phosphorus metabolism have led to contradictory conclusions.

Calcium balance studies, further investigation of the high alkaline phosphatase, bone and marrow biopsies were to be done when the family insisted on the boy's help on their farm.

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Psychologic Aspects of Pediatrics

PURE MATERNAL OVERPROTECTION

Maternal Overaffection

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THE term "overprotection" has been used to characterize the behavior of mothers whose devotion to their children is unusually intense.[1] They allow no competing interest to interfere with their maternal duties and they reduce their other relations in life, marital, social, intellectual, to a minimum.

CLASSIFICATION

Overprotective mothers may be divided into two groups, (1) pure and (2) guilt or compensatory. The "pure" group is made of women who display excessive care for a "wanted" child. The criterion of the "wanted" child is included in order to separate off those mothers who overprotect their children to mask or compensate for a hostility or rejecting attitude of which they are generally unaware.

In addition, there are mixed forms of overprotection and nonmaternal forms. The mixed group includes cases in which an early maternal overprotective attitude disappears later on, most commonly following the birth of a second child. The misbehavior of the older child, stemming directly from the early maternal oversolicitude, may lead to parental rejection. In such instances sibling rivalry is generally a major problem. Shifts in attitude are also seen when a child toward whom the mother had been indifferent suffers a dangerous illness which necessitates much nursing care on her part. In this group may also be included the mothers who, because of business or professional interests outside the home, try to make up for their hours of absence from the child through the intensity of their devotion while with him.

Nonmaternal forms of overprotection, especially by a grandmother living in the patient's home, are frequent. Such cases are often complicated when the young mother is herself not completely emancipated from the daughter relationship and her own marriage is thereby disturbed. The child may also be overprotected by the father, the siblings, the grandfather, other relatives living in the home, a nurse, etc. Marked paternal overprotection is rare, although favoritism, generally for a daughter, is common.

This review is limited to a discussion of pure maternal overprotection or maternal overaffection.

ETIOLOGY

The factors leading to pure maternal overprotection may be divided into three groups: (1) excessive maternal drive, (2) external factors, and (3) emotional privations.

From The Department of Pediatrics, New York University, College of Medicine.

1. Excessive Maternal Drive.—The essential feature of pure maternal overprotection is exaggeration of normal maternal behavior. The maternal drive varies in the same way as do all other biologic attributes. When calibrated along a scale of values, it shows a normal distribution curve with a small group of overaffectionate, overprotecting mothers at one end of the curve matched by a similar group of rather indifferent or rejecting mothers at the other end. The overprotecting mother represents a quantitative rather than a qualitative difference in response from the group of mothers as a whole. All the manifestations of the overprotecting mother will be found in a normal sampling of mothers but in milder degree. Similar variations in the intensity of the maternal drive have been observed in lower animal forms.[2]

That there is a hormonal basis for the maternal drive is indicated by experiments showing that the maternal feeling in animals can be strengthened by injections of pituitary extracts.[3] The specific hormone involved is prolactin.[3] It is interesting to note in this connection that a high degree of correlation ($r = .579$, P.E. $= .053$) has been established between the duration of the menstrual flow in women and the strength of the maternal drive, women with 6- and 7-day periods showing, on the average, higher scores than those with 2- and 3-day periods, while women with 5-day periods gave an intermediate average score.[4]

There are women who display strongly maternal instincts from early childhood. As children they like to play with and take care of dolls at an age when most girls lose interest in them. They seek out opportunities to take care of other people's babies and they fantasy about having large families. Their relations with boys are often "maternal." At the other end of the scale are the women who, as children, lose interest in dolls at an early age; who are not interested in babies and never fantasy about being a mother and having children.

Levy[5] negates the viewpoint, suggested by some investigators, that an exaggeration of the maternal instinct necessarily implies a neurosis. He believes that an intense maternal drive can be explained on the basis of innate variability, in most instances reinforced by external factors and emotional privations.

2. External Factors.—A long period of waiting for a child is a potent factor. Thus overprotection is frequent when the mother marries relatively late in life, when there is a long period of sterility, when there have been several spontaneous miscarriages, or when a child is adopted after a number of years of trying to have a child. A child is likely to be overprotected if the mother knows, for one reason or another, that she is not going to have more children. Death of a previous sibling or a dangerous illness in the patient himself, a physical or mental handicap, are also factors.

The type of illness in the child and the age of its occurrence are important considerations. As might be expected, an illness associated with alarming manifestations such as convulsions or shock is more likely to influence the mother than a more serious but less stormy illness. Illness in a young infant has a much greater and more lasting effect than when it takes place later on.

Sex difficulties between the parents reinforce maternal overprotectiveness. Levy points out that a wife devoted to her husband cannot be exclusively a

mother. On the other hand normal emotions, not finding an outlet in the interparental relations, may well be shunted in the direction of maternity. Absence of the father because of death, divorce, etc., acts in the same way as sex maladjustment. In only four out of the twenty cases of pure maternal overprotection studied by Levy did the marital relations appear normal. Lewenberg[6] found that sexual maladjustment was almost twice as common in overprotecting mothers as in other mothers.

Social life: There is little social life in common between the parents of overprotected children. This is not to be explained entirely on the basis of sexual incompatibility, since it has been found that many husbands and wives have an active social life together in spite of sexual disharmony. In many instances the overprotecting parent attributes the curtailment of social life to the need to be with the child.

3. Emotional Privations, especially lack of maternal love in early life, may create a craving for affection, thereby exaggerating the normal maternal drive. In Levy's series, lack of maternal love was a feature of the lives of most of the women.

Sex of the child: Overprotected children are predominantly boys. Nineteen of the twenty children in Levy's series were boys.

PERSONALITY OF THE OVERPROTECTING MOTHER

Overprotecting mothers are predominantly responsible, stable, and aggressive. As a group they are good managers, thrifty, reliable, competent. Relatives and friends often turn to them for help and advice. They generally give a story of steady employment before marriage. Aggression, in association with maternity, is seen in many animals, especially in fighting off enemies. It serves to protect the young.

Another prominent feature of the overprotecting mother is thwarted ambition. Many give a history of unfulfilled ambitions for education or a career and this, in turn, gives rise to strong ambitions for the education of the child.

THE PATERNAL ATTITUDE

The fathers of overprotected children are, as a group, submissive, stable husbands and providers who play little part in the rearing of the child. Any attempts which they may make to discipline the child are firmly resented by the mother. In none of Levy's twenty cases could the father be characterized as dominating. Discipline is left largely in the hands of the mother and whatever role the father assumes is determined principally by her. This pattern of behavior has been described as characteristic of American fathers in general. In the case of the fathers of overprotected children, however, the submissive role is exaggerated.

Although most fathers readily adjust to the maternal monopoly and maintain an affectionate relationship with the child, some resent their exclusion from participation in parenthood. They withdraw from the picture and refuse to attempt any disciplinary measures. Their attitude toward the child is then one of indifference or impatience. It is interesting to note that in none of Levy's

cases was there overt hostility. An added factor in some cases is the derogatory attitude of the child toward the father, which is fostered by the mother.

MATERNAL BEHAVIOR

Overprotection is evidenced in the behavior of the mother by (1) excessive care of the child, (2) excessive contact, (3) overprotection against the usual hazards of childhood, and (4) variations in the customary attitude toward training in the direction of overindulgence or domination.

Excessive care refers to the continuation of such activities as feeding, dressing, and bathing the child past the usual age. Breast feeding is apt to be unduly prolonged. The effect of this type of behavior is to retard the psychologic maturation of the child or to "infantilize" him. Excessive contact relates to the tendency of the mothers to remain in constant social relationship with their children. In some instances they continue to sleep with them even in their teens. The mothers manifest their overprotective attitude, further, by protecting the child against the ordinary risks of childhood. They limit the child's play with other children lest he hurt himself, learn bad habits, or contract a contagious disease. They accompany the child to school long after children of similar age are allowed to go alone, or they move near the school so that they can watch the child from the moment he leaves home until he enters school.

Training takes the form of one extreme or the other, indulgence or domination. There seems to be no middle position. Indulgent mothers yield to the demands of their children, allowing them to run riot without regard to the usual rules regarding mealtime, sleeping time, possessions, or organization of the household. The dominated children, on the other hand, are obedient, neat, careful, and polite. In the group as a whole, bladder control is established early.

PROBLEMS OF THE OVERPROTECTED

The problems of the children of overprotecting mothers may be classified into two groups, depending on whether the mothers are indulgent or dominating. According to Levy the principal factor determining the attitude of the mother is the personality of the child. His investigations show that submissive and aggressive behavior are manifested early in life and are most likely based on differences in innate endowment.

The children of overprotecting, overindulgent mothers have a difficult time in making social adjustments, the degree of difficulty being proportionate to the intensity of the maternal attitude. The children are, as a group, demanding, selfish, and tyrannical, anticipating constant attention, affection, and service. They respond to denials of their wishes or to the requirements of discipline with impatience and outbursts of temper or assault. When left alone they are restless unless they are immersed in a book. As a group they are gifted in conversation (owing to their constant association with grown-ups rather than children) and they use every device—charm, wheedling, coaxing, and bullying—to get their own way. This aggressive, demanding behavior of the overprotected has, as its primary aim, maintenance of the originally favored position

with the mother. It differs in this respect from the similar behavior of the emotionally deprived who appear to express in their constant demands for attention an insatiable hunger for things which they have missed.

The extent of the child's misbehavior is roughly proportionate to the parental response. The more the parents give in, the greater is the child's tyranny. In some instances it reaches the point where the child is outspokenly critical of his parents and abusive, or even physically cruel. Such can be the result of a home medium rich in love but poor in discipline.

The problems presented by the children of dominating, overprotecting mothers are principally shyness, anxieties, fears, and submissive behavior.

School.—The evidence of emotional instability is much more apparent in familiar than in unfamiliar surroundings. In contrast to their misbehavior at home, children of the indulgent, overprotected group as a rule give little trouble at school. Indeed, some of them are models of good behavior there and their teachers are often surprised to learn that they are difficult at home. When trouble does occur, it follows the pattern of misbehavior at home; impudence, disobedience, attention-seeking.

School performance is generally good in reading, language, dictation, history, and literature, owing to superiority in verbalization (as a result of constant association with adults), the mother's coaching, and restriction of conflicting play interests.[7] This superiority generally does not relate to mathematics, where reading ability and vocabulary have the least application.

The children usually like school because they are successful there and because they are temporarily, at least, free from maternal domination.

Friends.—Overprotected children have difficulty in making friends. The principal complaint is that they are too bossy and always insist on being the leaders. They are aggressive, cocky, selfish, and boastful. The mothers often interfere with play and friends. As a result of exclusion from the group and inability to be accepted on an equal status, they often seek as playmates younger children or girls. The difficulty in making friends tends to diminish with increasing age. Even young, overprotected children frequently make a good adjustment at summer camp after an initial period of unhappiness.

Outside Interests.—The principal outside interest of overprotected children is reading. As a rule they avoid rough-and-tumble activities and organized games. Hence the development of strength, agility, endurance, and muscle coordination suffer. Even more important, perhaps, is the loss in social relationships.

Undesirable Habits.—These are no more common in overprotected than in normal children. Feeding problems are perhaps more frequent; on the other hand enuresis is less common.

Sex problems are not notably frequent in overprotected children.

PHYSICAL STATUS

As a group, Levy found the overprotected children to be larger and heavier than other children attending the clinic, possibly owing to the excellent physical care which they had received. Only two of the twenty in his series might be

regarded as obese. Errors of refraction were frequent, possibly because of the excessive reading. Tonsillectomy was more frequent than in other groups.

TREATMENT

An effort should be made to give the mother insight into her overprotecting attitude and its effect on the child. The value of releasing the child from her infantilizing influence should be stressed. The father should be urged to take a more active interest in the family life, develop a friendly relationship with the child, and use his authority as a father.

Interests and activities for the mother outside the home should be encouraged and the parents should participate together in social activities such as visits, trips, vacations, etc. The child, if old enough, needs to realize the mechanism of infantile dependency and tyranny and the importance of behavior suitable to his age. The nursery school, play groups, outings with other children, summer camp, boarding school, are used in order to separate the child as much as possible from the mother.

In an appraisal of the therapeutic methods, Levy found that attempts to give the mother and the child insight into their behavior were of the least value. More useful were interviews with the father. The most effective methods were those which aimed at diluting the mother-child relationship through separating mother and child as much as possible and through stimulating maternal interest in social activities outside the home.

PROGNOSIS

The outlook for the future of the overprotected child is good. The end results of loving a child too much, though occasionally disastrous are generally benign. Once a gain toward independent activity is achieved, the child fights against the infantilizing tendencies of the mother. In this effort he is often assisted by the father. Moreover, the mother is generally willing to assist, also, since she finds relief in lessened responsibilitiy for the child.

Even without treatment, the natural process of maturation tends to release the child from the overprotective attitude of the mother. Merely going to school and being away from the mother for several hours a day are beneficial influences. The process of adolescence is an emancipating force. As adulthood is approached and close competition with colleagues in studies and games becomes less intense, a major factor in the difficult adjustment of the overprotected individual tends to disappear. Furthermore, with increasing age facility in conversation tends to make for popularity and these individuals are often the "life of the party."

PROPHYLAXIS

The most effective way of handling maternal overprotection is prophylactically. It can frequently be anticipated when the "external factors" discussed under "etiology" (a long period of waiting for a child, death of a previous child, earlier, serious illness of the patient, adoption) are operative. Where the child has a physical or mental handicap the mother can be expected to be

overprotective. The whining, demanding, self-centered behavior of many handicapped individuals is directly attributable to parental mismanagement. Not infrequently great assistance can be rendered such cases by repeatedly emphasizing the dire effects of overprotection and the added barrier raised thereby against normal adjustment. In many instances the only treatment of value is psychologic. Even in the absence of these contributing factors it is a simple matter for the pediatrician, who sees the mother and child repeatedly, to recognize excessive maternal drive. In such instances appropriate measures should be instituted before the maternal attitude has become fixed.

SUMMARY

1. Pure maternal overprotection or overaffection is a quantitative rather than a qualitative deviation in the maternal drive.

2. It is to be distinguished from "guilt" or "compensatory" overprotection where the maternal overprotectiveness represents an effort to conceal a rejecting attitude of which the mother is generally unconscious.

3. An innately determined strong maternal drive is generally reinforced (1) by external circumstances, such as a long period of anticipation, serious illness of the child, a physical or mental handicap, and (2) by maternal emotional privations in childhood.

4. Mothers manifest their overaffection by excessive care of the child, excessive contact, overprotection against the usual hazards of childhood, and variations in the customary attitude toward training.

5. Behavior of the child depends on whether the mother is indulgent or dominating. If the mother is indulgent the child is demanding, selfish, and tyrannical. If the mother is dominating the child is shy, anxious, fearful, and submissive.

6. The most effective methods of treatment are those which aim at separating mother and child.

7. The outlook for the future adjustment of the overprotected individual is good. Most develop into well-balanced adults.

8. By early recognition of the circumstances which may lead to overprotection it is possible to institute appropriate measures before the maternal attitude has become fixed.

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Comments on Current Literature

VIRUS ENCEPHALITIS

THE importance of arthropod vectors in the epidemiology of virus encephalitis is becoming increasingly apparent. Papers published in the last ten years report field and laboratory studies which indicate clearly that the tick, the mosquito, and the mite may act as vectors for the viruses of encephalitis, and that these arthropods are potentially capable of playing a significant rôle in the natural history of the summer encephalitides. Of particular interest are the arachnid vectors, the tick and mite, which have been shown capable of passing the viruses of St. Louis encephalitis and of western equine encephalomyelitis transovarially to their offspring.

In a recent article in the *Proceedings of the Society for Experimental Biology and Medicine*,[1] Howitt, Dodge, Bishop, and Gorrie report the isolation of the virus of eastern equine encephalomyelitis from chicken mites, *Dermanyssus gallinae*, and from chicken lice, *Eomenacanthus stramineus* and *Menopon pallidum*. The mites were collected from a chicken house near Shelbyville, Tenn. In several areas of central Tennessee, sporadic cases of encephalitis in children had been reported during the summer of 1947. Chicken mites collected in August, 1947, were triturated in a mortar with 3 c.c. of buffered saline containing 30 per cent normal rabbit serum. After centrifugation the supernatant fluid was injected intracerebrally and intraperitoneally into 12-day-old Swiss mice. A filtrable virus was isolated which was identified by appropriate studies as the virus of eastern equine encephalomyelitis. This isolation represents the first instance that the virus of eastern equine encephalitis has been recovered from an arachnid in nature.

The virus of eastern equine encephalomyelitis was isolated also from chicken lice collected on a farm near Alexandria, Tenn. Since the chicken louse, a member of the order Mallophaga has mouth parts adapted not for sucking but for chewing the surface of the skin and feathers, the authors point out that chicken lice have been observed to feed on young feathers from which the dermal papillae bearing blood vessels, have not yet withdrawn, thus making the drawing and ingestion of blood by the chicken louse possible.

Demonstration of type-specific antibody to the eastern strain in a few chickens and in a single cow from this area seems a significant finding.

The isolation of the virus of eastern equine encephalomyelitis particularly from chicken mites is of considerable interest in light of the findings of other workers in this field. During a nonepidemic year, the virus of St. Louis encephalitis was isolated from chicken mites, *Dermanyssus gallinae*, collected in three widely separated chicken houses in St. Louis County.[2-5] Sulkin[6] isolated the virus of western equine encephalomyelitis from chicken mites, *Dermanyssus gallinae*, in Dallas County, Texas. Reeves, Hammon, and their coworkers[7] isolated the western equine virus from bird mites, *Liponyssus sylviarum*, collected in Kern County, Calif. More recently this group of investigators has reported the isolation from bird mites of a mixture of the virus of St. Louis encephalitis and western equine encephalomyelitis virus.[8] Sulkin and Izumi[9] recovered the western equine virus from the tropical bird mite, *Liponyssus bursa*.

The isolation of the viruses of St. Louis encephalitis, western equine encephalomyelitis, and now, eastern equine encephalomyelitis, from mites collected in nature, suggests strongly that this arachnid vector plays an important rôle

in the natural history of the summer encephalitides. In the case of St. Louis encephalitis,[4] it has been shown that transovarial passage of the virus is possible, and that colonies of chicken mites found infected in nature or infected experimentally in the laboratory, harbor the virus for at least two years. It has been demonstrated further[10] that viremia occurs in chickens as a result of the bite of infected mites, and that mites or mosquitoes feeding on such chickens during the period of viremia not only acquire virus but are capable of transmitting the virus by bite to other chickens and to mammals. Mosquitoes infected in this manner are capable of transmitting the virus to chickens and to hamsters.

It will be of considerable interest to follow reports concerning possible transovarial transfer of the virus of eastern equine encephalomyelitis in mites. Of interest likewise will be experiments designed to demonstrate whether mosquitoes feeding on chickens having viremia as the result of the bite of infected mites can acquire the virus and subsequently transmit the virus by bite.

Such a concept of epidemiology, involving two blood-sucking vectors, an arachnid capable of transovarial passage, the reservoir in nature, and an insect, probably the mosquito, capable of transmitting the virus to mammals, including man, would serve to explain some of the unique features of the natural history of the summer encephalitides. Since all three viruses, St. Louis encephalitis, western equine encephalomyelitis, and eastern equine encephalomyelitis, have been isolated from mites collected in nature, it seems possible that similar factors may be involved in the epidemiology of these three virus diseases.

RUSSELL J. BLATTNER.

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News and Notes

Dr. Frederic H. Bartlett of New York died October 19 of a heart attack. Although Dr. Bartlett was 76 years old, he had continued in active practice and had been at his office the previous day. He was for many years attending physician at the Babies Hospital and a member of the faculty of the College of Physicians and Surgeons. He was a member of the American Pediatric Society and served as vice-president in 1937.

Dr. Lendon Snedeker of Boston has retired from active practice to become assistant administrator of the Children's Medical Center of Boston.

Vanderbilt University School of Medicine announces that Professor Arvid Wallgren, of Stockholm, Sweden, will be the next Abraham Flexner lecturer. Dr. Wallgren will arrive in the United States about March 1, 1949.

The original announcement of this Lectureship was made in the fall of 1927 when Mr. Bernard Flexner, of New York City, gave fifty thousand dollars to Vanderbilt University for the purpose of establishing the Abraham Flexner Lectureship in the School of Medicine. This Lectureship is awarded every two years to a scientist of outstanding attainment who shall spend as much as two months in residence in association with either a department of a fundamental science or of a clinical branch. Previous lecturers have been:

Dr. Heinrich Poll, Director of the Institute of Anatomy of the University of Hamburg, Germany.

Sir William B. Hardy, Director of the Low Temperature Research Station at Cambridge University, England.

Dr. Francis R. Fraser, Director of the Medical Unit and Professor of Medicine at the St. Bartholomew Hospital and Medical School, London, England.

Dr. Erik Gunnar Nystrom, Professor of Surgery at the University of Uppsala, Sweden.

Dr. Thorvald Madsen, Director of the State Serum Institute of Denmark.

Dr. Albert Szent-Gyorgyi, Professor of Medical Chemistry and Director of the Institute for Medical Chemistry in the Royal Hungarian Franz Joseph's University, Szeged, Hungary.

Dr. Donald D. Van Sloke, member of the Rockefeller Institute and Dr. Warfield T. Longcope, Professor of Medicine, Johns Hopkins School of Medicine.

Sir Edward Mellanby, Secretary of the British Research Council and Chairman, International Technical Commission on Nutrition.

Dr. Wallgren has been Associate Professor of Internal Medicine at Uppsala University and Head of Pediatrics at the Royal Caroline Medical Institute since 1942. He is an Honorary Member of the American Academy of Pediatrics; Canadian Association for the Study of Children's Diseases; Argentine Pediatric Society; and German Pediatric Society. He is co-editor of Acta Paediatrica and a member of the Editorial Board of Annales Pediatrici; Pediatria Danubiana; Acta Tuberculosea; Archiv für Kinderheilkunde. He is president of the Swedish Association for Children's Welfare; the Swedish Red Cross Committee on Tuberculosis; the National League Against Tuberculosis; the Save the Children Fund; and Conseiller to the State Board of Public Health.

He is widely known in Europe and the United States for his pediatric writings which include over two hundred papers in the field of pediatrics and child health.

The **Rochester Child Health Institute** announces two assistantships of one year each; one beginning the first of January and one the first of July of each year. These services include preventive medicine in pediatrics with the opportunity of studying normal growth and development, care of the newborn, well child care, psychological problems in young children and school examinations. These are equivalent to fellowships in the sense that opportunities for both service and research are given. The stipend of $1,620 is offered to suitable candidates. The first available fellowship will be Jan. 1, 1950.

Book Reviews

Psychiatry for the Pediatrician. Hale F. Shirley, M.D., New York, 1948, The Commonwealth Fund, 442 pp. Price $4.50.

This book is an outgrowth of lectures given by Dr. Shirley to medical students at Stanford University. In its expanded form it is addressed to the large professional audience of pediatricians and general practitioners who are interested in better methods of child guidance in their own practices and who need a comprehensive, yet simple, guide in this field. The author has made a particular effort to suit his text to his audience. He avoids theories and unsettled controversies and shelves involved psychiatric terminology in favor of simple English. He makes a liberal use of case histories. The result is a thoroughly readable book.

The various types of psychiatric problems are covered one by one, and there is an adequate index. However, this book is not primarily intended to be a reference book to which the pediatrician will refer when he encounters a given case. The author intends, rather, that it be read through, and hopes that in doing so the reader will gain a point of view along with a practical foundation of knowledge upon which he can build. After a brief but lucid discussion of basic principles of psychiatry and child guidance, there is a section on development and habit training, followed by a detailed consideration of the role in childhood behavior disturbances of: physical factors, intellectual factors, emotional factors, sexual factors, and environmental factors. There is a wealth of practical information in these chapters. Finally, the author concludes with two chapters on the investigation and treatment of behavior problems.

In order to gain perspective for this presentation, Dr. Shirley reviewed the records of the first 1,000 patients seen in the Stanford University pediatric-psychiatric unit. As a result the choice of material has a foundation in practical experience. It represents, however, the practical experience of a psychiatric clinic, which perhaps explains the dearth of space given to the preventive mental hygiene aspects of ordinary practice.

Dr. Shirley does not attempt to define the limitations of the practitioner in handling these problems in children. He believes that a great deal can be accomplished by those who have the interest and who will take the time to learn the fundamentals. His book should be a great help to this group.

BAKWIN

Stethoscopic Heart Records, Columbia Album No. CM-735 (Revised). George D. Geckeler, M.D.

The set consists of four, double-faced records, on which are recorded auscultatory cardiac findings. Normal heart sounds are frequently repeated for comparison with abnormal sounds. Practically all types of abnormal cardiac sounds are recorded, especially the arrhythmias. The various types of abnormalities are described by a preceding commentary.

The sounds and descriptions are very clear. These recordings should be of interest to all physicians and particularly to medical students and teachers. They should be especially suited to group teaching.

CARSON

Hearing and Deafness: A Guide for Laymen. Edited by Hallowell Davis, M.D., Director of Research, Central Institute for the Deaf, and Research Professor of Otolaryngology, Washington University School of Medicine, St. Louis, Mo. Illustrated. New York, 1948, Murray Hill Books, Inc., 468 pages. Price $5.00.

Of the 30,000,000 children of school age in the nation, some 18,000 are totally deaf, and "our best estimate is that from 1,500,000 to 2,000,000 children in the United States have defective hearing." The *raison d'être* for this excellent collection of articles which deal with the problems of the deaf and hard-of-hearing is thus clearly established. For Dr. Davis "audiology" is truly "a meeting of varied specialists." He has brought together, in one volume, physician, speech educator, speech therapist, teacher for the deaf, psychologist, and field worker to explain to the doctor and his patient the problems which confront the acoustically handicapped individual. The fourteen collaborators cover the field in a thorough fashion.

The title of the book is unfortunate, for the pediatrician can profit from a reading of it. The techniques of audiometry, both the pure tone and work-sentence types, are discussed. The importance of an early diagnosis of defective hearing and an early start in speech training and in *speech conservation* is emphasized. "The confusions caused by imperfect hearing often lead to a progressive deterioration of the ability to discriminate (various sounds). . . . In consequence, every acoustically handicapped child who can benefit from a hearing aid should be fitted with his own instrument as soon as he is ready for it." Education should begin at the nursery school level and should be approached from the oral point of view, as the authors definitely feel "that it is possible, practical, and desirable to teach even totally deaf children to speak and to read speech." Despite the severity of the handicap, recent studies at the Central Institute for the Deaf have shown an educational retardation of only two to three years among their pupils. The problems of the older child and the adult with acquired hearing defects which have to do with the choice of a vocation and the attainment of social maturity are freely discussed. Attention is directed toward the important role of the ever-present, but seldom realized, *auditory background* in our daily lives. Methods of speech reading, of auditory and speech training, both for child and adult, are pointed out. More emphasis could have been placed on the usefulness of similar methods of speech training in the treatment of the acoustically normal child whose articulation is faulty.

The volume can be recommended for patient and parent. The chapters on the medical and surgical aspects of deafness are very well written from the layman's point of view; those on hearing aids should be helpful, and the discussions of educational methods, vocational problems, psychology, and organizations for the deaf will be interesting to him. Much of the material, however, particularly that on the physics of sound perception, anatomy of the ear, vacuum tube circuits, and the interpretation of audiograms, may be beyond his reach. In all, the book should be more readily appreciated by the physician and by those who deal with the problems of the deaf.

FORBES.

Handbook of Orthopaedic Surgery, ed. 3. A. R. Shands, Jr., St. Louis, Missouri, 1948. The C. V. Mosby Company. Price $6.00.

The first edition of this excellent handbook on orthopaedic surgery was particularly designed to present the fundamental facts and principles of orthopaedic surgery to the medical student and the general practitioner. It served this purpose well, and the third edition will continue to do so. The essential points in etiology, pathology, diagnosis, and treatment of all of the conditions embraced by orthopaedic surgery, except fresh fractures, are covered in such a manner as to make the book an excellent source of reference for physicians in every specialty, particularly pediatrics. An outstanding feature of all editions has been the excellent bibliography which is arranged uniquely according to subjects discussed in each chapter. This permits references to be quickly obtained on any subject. The bibliography in this third edition has been brought up to date so that articles published as late as 1947 are included. The book is strongly recommended for the purpose for which it was originally intended.

HAMPTON

Editor's Column

MR. EWING'S REPORT TO THE PRESIDENT

THE unexpeeted and amazing victory of President Truman on November 2, which swept into power a Congress of his own party, is a mandate of the people for legislation putting into effect the principles and proposals upon which he based his campaign. This is the very essence of democracy and of our political system. One of the important proposals made by the President was extension of social security and better medical care for the American people.

In light of this, our thoughts have turned to the report of Oscar R. Ewing, Federal Security Administrator, which was published last September, entitled "The Nation's Health, a ten year program."

In January of this year the President asked Mr. Ewing ". . . to undertake a comprehensive study of the possibilities for raising health levels and to report to me, at your early convenience, upon feasible goals which might be realized by the American people in the next decade." As a part of the study, Mr. Ewing called the National Health Assembly which met in Washington last May, and much of the report is based on the findings of the Assembly. On the issue of national health insurance agreement could not be reached, and Mr. Ewing in his report sides with the proponents. This was quite within his rights and in keeping with his previous statement that his report would not be bound by the findings of the Assembly.

We have refrained from commenting on the report previously as it has been claimed that it was a politically inspired document and campaign propaganda. Regardless of all this, in our opinion it is today, in light of the November election, a document of vital importance to the physician, as beyond question it presents the plan in a broad way upon which proposed legislation will be based in the next Congress. We urge every physician to read the report so that he may have a first-hand idea of the medical legislation which will be proposed. It may be obtained from the Superintendent of Documents, U. S. Government Printing Office, Washington, D. C., price $1.00.

B. S. V.

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